University of Alberta

Evaluating Involuntary Weight Loss in Head and Neck Cancer Patients

by

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ABSTRACT

Involuntary weight loss is a common issue of cancer patients, especially those with head and neck cancer. Successful management of involuntary weight loss relies on early systematic identification of nutritional risk and treatment of the underlying causes.

The Patient Generated Subjective Global Assessment (PG-SGA) nutrition screening tool was used to evaluate the nutrition status of head and neck cancer patients (n=350) prior to treatment. Prior to treatment, over half (55%) of the patients were at nutritional risk (PG-SGA score $\geq$4) and of those at risk, 30% (107/350) were in critical need of nutritional intervention (PG-SGA score $\geq$9). Forty-eight percent of the patients had Grade 1 weight loss (weight loss of 2-5% in 6 months) at presentation. Additionally, 44% of the patients had $\geq$2 symptoms and 47% of patients rated their functional capacity as reduced. No appetite, problem swallowing, pain, and taste changes were significant predictors of reduced dietary intake. Symptoms may play a role in reducing dietary intake of head and neck cancer patients prior to treatment.

Self-report and objective measures were used to evaluate the relationship of symptoms to energy intake, weight loss, functional performance, and quality of life of head and neck patients over time. Systemic inflammation and symptoms were predictors of energy intake, weight loss, and functional performance of patients receiving adjuvant chemotherapy, but only symptoms were predictors of outcomes in patients not receiving adjuvant chemotherapy. The understanding that symptoms contribute to the decline of energy intake, weight loss, functional performance, and

quality of life over time may help in the development of appropriate symptom management, including nutrition support to prevent weight loss in head and neck cancer patients.

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List of Abbreviations

~	approximately
AIDS	acquired immune deficiency syndrome
ANOVA	analysis of variance
BMI	body mass index
BW	body weight
CI	confidence interval
cm	centimeter
CRP	C-reactive protein
CTCAE	Common Terminology Criteria for Adverse Events
d	day
dl	deciliter
ECOG	Eastern Cooperative Oncology Group
ESPEN	European Society for Clinical Nutrition and Metabolism
GEE	Generalized estimating equations
gm	gram
Gy	grays
HNC	head and neck cancer
HR	Hazard ratio
ICD	International Classification of Diseases
IL-1	interleukin-1
IL-6	interleukin-6

kcal	kilocalorie
kg	kilogram
m^2	meters squared
mg	milligram(s)
min	minute
ml	milliliters
mm^3	milliliters cubed
MNA	Mini Nutrition Assessment
MST	Malnutrition Screening Tool
ONS	Oncology Nursing Society
P-alb	pre-albumin
PG-SGA	Patient Generated Subjective Global Assessment
PINI	Prognostic Inflammatory and Nutritional Index
QOL	quality of life
RT	radiotherapy
RTchemotherapy	concomitant radiotherapy and chemotherapy
S-alb	serum albumin
SE	standard error
sec	second
surgery RT	surgery followed by radiotherapy
surgery RTchemotherapy	surgery followed by concomitant radiotherapy and chemotherapy
T1	tumour < 2 cm
T2	tumour ≥ 2 cm but ≤ 4 cm

T3	tumour ≥ 4cm
T4	tumour of any size with invasion to adjacent structures
TNFα	Tumour necrosis factor alpha
UWQOL	University of Washington Quality of Life revised questionnaire
WCCNR-SSS	Western Consortium of Cancer Nursing Research Stomatitis Staging System
WHO	World Health Organization
wt	weight

Chapter 1 Evaluating Involuntary Weight loss in Head and Neck Cancer Patients

1.0 Introduction

1.1 Background

Involuntary weight loss is common in cancer patients, adversely affecting quality of life and survival. Individuals with head and neck cancer are particularly vulnerable to involuntary weight loss.[1,2] This thesis addresses a gap in our current understanding regarding factors affecting weight loss in individuals with head and neck cancers and provides a foundation for nutrition-related interventions intended to reduce weight loss and improve clinical outcomes in this population.

1.2 The Epidemiology of Head and Neck Cancer

Head and neck cancers account for 5-6% of all cancers diagnosed in Canada,[3] representing a heterogeneous tumour group that includes lip and oral cavity, pharynx, larynx, paranasal sinuses, salivary glands, and thyroid gland.[4,5] Approximately 80-90% of head and neck malignancies are squamous cell carcinomas, with the remaining 5-7% being adenocarcinoma or adenoid cystic carcinomas.[4-6] Women in Canada have a lower incidence compared to men for tumours of the lip and oral cavity, pharynx, larynx, paranasal sinuses, salivary glands but are 4 times more likely to have tumours of the thyroid gland.[3] The overall standardized incidence rate in Canada has been estimated at 13.0 per 100,000 in men and 5.0 per 100,000 in women for oral cancer.[3] The relative 5 year survival for oral and laryngeal cancer is 63% and 64%, respectively.[3] Tobacco, alcohol, wood dust, asbestos, and chemical exposure, Epstein-Barr virus, Human papillomavirus, and $\geq$ 45 years of age are risk factors for head and neck cancer.[6,7]

1.3 Factors Associated with Involuntary Weight Loss in Head and Neck Cancer

Head and neck cancer patients frequently experience involuntary weight loss, and ≥ 10% weight loss is reported to affect 30- 50% of those with advanced head and neck cancer.[1,2] In the literature the terms "involuntary weight loss" and "cachexia" are used interchangeably, but these may be separate or related phenomena.[8] For the purposes of this dissertation, involuntary weight loss is considered an umbrella term.

Involuntary weight loss can be attributed to two key components: systemic hypermetabolism/hypercatabolism and reduced food intake.[9-10] In addition to involuntary weight loss, patients with cachexia generally present with asthenia, sarcopenia, anemia, and anorexia - all of which may lead to compromised functional ability. Involuntary weight loss is associated with increased treatment toxicities and complications, treatment delays, lengthened hospital stays, and increased mortality and morbidity.[11-14] Cancer patients' prognoses and responses to treatment are directly related to the rate and degree of body weight loss.[15] The loss of as little as 5% body weight over six months increases the incidence of treatment complications in cancer patients.[15]

Involuntary weight loss due to hypercatabolism/ hypermetabolism

The hypercatabolic/hypermetabolic mechanisms related to cachexia include elevated hepatic glucose production, reduced glucose utilization by peripheral tissues, increased Cori cycle activity, and insulin resistance.[16,17] Additionally, increased proteolysis and decreased protein synthesis by skeletal muscle leads to a loss in lean tissue mass.[18] Alterations in lipid metabolism including lipolysis, decreased lipid

production, and increased elevated triglycerides accelerate the loss of fat tissue.[17,18] Many of these changes are attributed to the presence of systemic inflammation.[17,18] Tumour necrosis factor (TNF-α), interleukin (IL)-1, IL-6, and interferon-γ may cause anorexia, increased proteolysis, and increased energy expenditure leading to loss of muscle tissue.[16-18]

Involuntary weight loss due to mechanisms of reduced food intake

Physiological, psychological, and social stimuli normally promote food intake.[19] The reduced food intake associated with cachexia can be primarily attributed to a disturbance of appetite control in the hypothalamus,[9,18] and secondarily, to the effects of the symptoms which constitute barriers to food intake.[9]

Both cancer patients and researchers have noted that certain symptoms such as nausea, vomiting, diarrhea, anxiety, constipation, taste changes, depression, and pain, referred to here as **nutrition impact symptoms,** interfere with the stimuli that promote food intake.[8,9,20-22] The nutritional status of individuals with head and neck cancers is further compromised by a number of additional factors. For example, demographic characteristics associated with this population, such as a poor social environment, excessive smoking and alcohol intake, may reduce dietary intake.[23-25] In addition, symptoms associated with head and neck cancer *per se* and with its treatment, such as swallowing difficulty, mouth sores, dry mouth, dental problems, and chewing difficulty, influence the functional ability to eat.

1.4 Supplementary Feeding in the Context of Involuntary Weight Loss

While lifesaving treatment regimes for head and neck cancer including surgery, radiotherapy, chemotherapy or a combination of these treatments have effectively improved head and neck patient's survival with the current overall 5 year survival rate at ~ 60%,[3,26] they also significantly compromise oral intake. This development has lead to discussions in the literature regarding whether to supplement oral intake and if so, when and how this feeding should be undertaken. Some authors have advocated feeding tube placement in order to forestall weight loss and prevent treatment interruptions due to declining nutrition status. Currently, the decision regarding the best time for feeding tube placement varies from prophylactic placement to placement only when oral intake cannot be attained. Some factors that have contributed to the controversy surrounding the timing of feeding tube placement stem from the limited success feeding tubes have demonstrated in preventing weight loss and treatment interruptions;[27-33] the concern that feeding tube placement and limited oral intake may result in long-term functional impairment to swallowing;[34] and poor 5-year overall survival.[35]

Alternatively, the decision to not provide adequate nutritional support can potentially leave patients with persistent and unresolved issues related to weight loss and nutrition impact symptoms.[36-41] Unfortunately, unresolved issues related to weight loss and nutrition impact symptoms have also been associated with reduced survival and effectiveness of treatment,[42] as well as markedly reduced quality of life,[43] and discontinued employment.[44]

1.5 Statement of the Problem

Although involuntary weight loss is reported to occur frequently in head and neck cancer patients and is an important factor in patient outcomes, a recent review suggested that the true incidence of malnutrition in the population is unknown.[45] Studies that have evaluated the nutrition status of head and neck cancer patients, have been hampered by retrospective designs, and small or discrete tumour or treatment.[12,13,46-51] But more importantly, many of these studies did not use a standardized method to assess nutrition status and define malnutrition. In order to determine the incidence of malnutrition and to successfully identify patients who would benefit from nutritional care and intervention, standardized definitions and nutritional screening tools are required.

Nutritional care and intervention is also limited by lack of knowledge regarding the impact of symptoms on dietary intake in individuals with head and neck cancer. To date the impact of symptoms on dietary intake has not been reported. McCallum[52] (2000) suggests that "Aggressive identification and treatment of nutrition-related symptoms can stabilize or reverse weight loss in 50-80% of oncology cases" (p.11). Without this information it is difficult to prevent reduced dietary intake associated with symptoms or to assess the impact of interventions designed to improve intake. A few studies have characterized weight changes and nutrition impact symptoms in head and neck cancer patients prior to treatment.[53-56] Nevertheless, these studies do not provide a clear picture of the most prevalent symptom-related barriers to food intake nor do they identify the symptoms having the strongest associations with reduced food intake. Published work has focused on discrete patient groups (ie) those

patients commencing radiation therapy,[2] or has included only a few patients with tumours localized in the oral cavity,[53] and less on population – based or representative samples of the tumour group. Also, the scope of symptoms studied varied, thus limiting discrimination of specific symptom issues.[2,53] Although a few authors have evaluated the impact of symptoms on weight loss or dietary intake across the trajectory of treatment,[36,48,43,46,49,54-56] these studies, were hampered by retrospective design, discrete patient groups, use of functional/subjective swallowing assessments to measure dietary intake, and diverse definitions of malnutrition.

The impact of head and neck cancer and its treatment on patients is profound. Involuntary weight loss significantly influences head and neck patient survivorship. Furthermore, enteral feedings has limited success in abating weight loss, treatment delays, and survival. Therefore, other interventions must be considered to address the fundamental issues around eating. Providing comprehensive care requires reliable and consistent assessment of nutrition status and the symptoms associated with the decline in nutrition status at the time of diagnosis and throughout the treatment trajectory.

1.6 Organization of this Thesis

This thesis seeks to improve understanding of the nutrition status of patients with head and neck cancer. Additionally, it seeks to improve our understanding of weight loss in head and neck cancer patients by exploring symptoms associated with reducing dietary intake. The results of the studies completed are presented as three papers (Chapters 2-4). In Chapter 2, I critically evaluate the three nutrition screening tools currently recommended by the Oncology Nursing Society. I recommend that the

Patient Generated Subjective Global Assessment (PG-SGA) nutrition screening tool be used by nurses to proactively assess for malnutrition among oncology patients. In Chapter 3, I describe the prevalence of symptoms that directly influence dietary intake, weight, and reduced functional capacity, the relationship between symptoms and dietary intake, weight loss, and reduced functional capacity in head and neck cancer patients, who had not started treatment. In Chapter 4, I describe the impact of treatment on symptoms (chemosensory function, mucositis, xerostomia, and swallowing), weight, dietary intake, and quality of life, as well as, the relationship between symptoms and dietary intake, weight, and quality of life during the treatment trajectory in head and neck cancer patients. In Chapter 5, I conclude by discussing the implication of this research for clinical practice, nursing education, policy, and future research.

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CHAPTER 2 CRITICAL EVALUATION OF NUTRITION SCREENING TOOLS RECOMMENDED FOR ONCOLOGY PATIENTS*

2.1 INTRODUCTION

Progressive weight loss and decline in nutrition status are significant problems in patients with cancer.[1,2] Current studies indicate that between 20–80% of oncology patients develop malnutrition over the course of their illness.[3-8] Malnutrition can have deleterious effects for oncology patients. DeWys et al.[9] found cancer patients with as little as a 5% weight loss at the time of diagnosis compared to those with no weight loss had poorer survival, chemotherapy response, and performance status. Vigano et al.[10] reported that advanced cancer patients have a reduced survival with a weight loss of greater than 8.1 kg in the previous 6 months. Furthermore, oncology patients who develop malnutrition during the course of their illness are at risk of having treatment complications and delays, frequent hospitalizations, and reduced quality of life.[6,9,11] McClement, Degner, and Harlos[12] examined families of palliative cancer patients and found that both family members and patients experienced numerous losses including lost opportunities to eat and commune together, altered body image, and altered role function as a consequence of weight loss and reduced dietary intake. Therefore, a decline in nutrition status is not only problematic for the patient and their family, but also increases health care costs.

Consequently, the early detection of malnutrition and provision of nutrition support for oncology patients is recommended by numerous clinical oncology practice groups, including the Oncology Nursing Society (ONS).[13]

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The ONS recommends that nurses in clinical practice: (a) complete nutrition screening of oncology patients at baseline and throughout the care process, (b) complete nutrition care plans for malnourished patients, (c) provide care which will prevent weight loss and reduce symptoms of malnutrition, (d) evaluate nutrition care plans and modify plans as required, and (e) provide specialized nutrition support for patients receiving antineoplastic therapy or those who have ingestion or absorption problems for a prolonged period. Additionally, the guidelines suggest that nurses should receive additional training and education on nutrition status in cancer including nutrition screening tools, nutrition care plans, and specialized nutrition interventions.

Traditionally, the responsibility for nutrition assessment of patients falls to dieticians. However, many cancer centers do not have any or only a few dieticians on staff to provide nutrition care.[14] Currently, nurses assess oncology patients on admission to hospital or to ambulatory clinics at cancer centers, which puts them in an ideal position to carry out nutrition screening. The purpose of nutrition screening is to identify those patients who require a more comprehensive nutrition assessment and subsequent nutrition support. As a result, a number of nutrition screening tools have been developed. However, only three are recommended by the ONS for use with oncology patients.[13] The aim of this paper is to critically evaluate the three recommended nutrition screening tools for use by clinicians in an oncology setting.

2.2 Method

The electronic data bases, CINAHL, PUBMED, and MEDLINE, were searched from 2000-2006 for English language articles. The search terms of Patient Generated-

Subjective Global Assessment (PG-SGA), Mini Nutrition Assessment (MNA), Malnutrition Screening Tool (MST), cancer, nutrition, and nutrition screening tools were used. Full text of articles were obtained when abstracts described the PG-SGA, MNA, MST, nutrition screening, and cancer patients. Additionally, a hand search through reference lists of retrieved articles was done. The articles reviewed included 23 empirical reports, 4 reviews, and 3 reports from professional associations.

2.3 Nutrition Screening

Nutrition screening is the process of identifying patients who are at risk for developing malnutrition or who are malnourished. Klein et al.[15] stated that the goals of nutrition assessment are not only to identify patients who are at risk of developing malnutrition or who are malnourished but also "… to quantify a patient's risk of developing malnutrition-related medical complications, and to monitor the adequacy of nutrition therapy" (p 134).[15] Thus, nutrition assessment refers to a comprehensive assessment that uses medical and diet history, physical examination, anthropometric measurements, and laboratory data to determine nutrition status.[14] The most common indicators used to assess nutrition status are included in Table 1. However, there is no "gold standard" for determining nutritional status because indices used are affected by multiple factors including disease and treatment. This makes it difficult to isolate the effects of malnutrition on clinical outcomes.[15,16] For example, body weight can be confounded by age, edema, dehydration, and tumour growth.[16] Therefore, it is recommended that more than one indicator be used to assess nutrition status to offset the shortcomings of any one indicator. Generally, nutrition screening tools use both subjective and objective data including height, weight history, current symptoms,

disease stage, and presence of co-morbidities to determine risk or presence of malnutrition. The following nutrition screening tools have been recommended for use in clinical practice by the ONS: the Patient Generated- Subjective Global Assessment (PG-SGA), the Mini Nutritional Assessment (MNA), and the Malnutrition Screening Tool (MST) (ONS, 2006).

Effective nutrition screening tools should be flexible and easy for clinicians to use and interpret.[17,18] Additionally, nutrition screening tools must demonstrate validity and reliability within the patient population[18,19] and must also be sensitive and specific for detecting risk and presence of malnutrition.[18,19] Furthermore, a nutrition screening tool should also direct clinicians in a plan for future nutrition care.[17] Finally, use of a nutrition screening tool should demonstrate a benefit to clinical outcomes.[17,18] Using these criteria, the three recommended nutrition screening tools are reviewed for their use by clinicians in oncology clinical practice.

2.3.1 *Patient Generated Subjective Global Assessment (PG-SGA).*[20] The PG-SGA was developed primarily to identify oncology patients who are at risk of developing malnutrition. It is an adaptation of the Subjective Global Assessment (SGA) [21] tool developed and validated for use with acute care patients. The PG-SGA consists of two sections. The first section is completed by the patient and includes data on weight history, food intake, symptoms, and activity level. A numerical score from this section can be used to triage patients requiring nutrition intervention. A score from 0-1 indicates that no intervention is required and that the patient should be re-assessed on a regular basis. A score of 2-3 indicates that the patient requires nutrition education by a dietician or nurse and pharmacologic management of symptoms. A

score of 4-8 requires intervention by a dietician or nurse and pharmacologic management of symptoms. A score ≥ 9 indicates a critical need for nutrition intervention by a dietician. The second section is completed by the clinician and includes a physical assessment, assessment of metabolic stress, and assessment of disease related nutrient demands. The second section categorizes the patient as well nourished (A), moderately malnourished or suspected malnutrition (B), or severely malnourished (C). Both subjective and numerical scores can be used to determine nutrition status and direct intervention. The PG-SGA is available in English, Norwegian, Spanish, and Swedish. Training is required to score the patient generated section, as well as to complete the clinical assessment portion of the PG-SGA. The Oncology Practice Group of the American Dietetic Association has produced a training video to assist clinicians in the use of the PG-SGA.[14] Several studies between 2000 and 2006 have used the PG-SGA to determine prevalence of malnutrition within various cancer populations including colorectal, urologic, pancreatic, head and neck, and lung.[4-7,11,22-28]

Ottery[20] originally stated that the clinical assessment portion of the PG-SGA added < 1 minute to overall screening time. However, mean screening time was not reported. Other researchers have reported that the PG-SGA is flexible for use with both in- and out-patients, is easy for both clinicians and patients to use, and reduces overall assessment time. However, formal evaluation of the tool's flexibility and ease of use has not been conducted.[7,26] Persson et al.[26] and Segura et al.[7] reported that both patients and personnel found the PG-SGA simple to complete. However, Persson et al.[26] stated that patients had difficulty recalling their weight in the previous year.

Read et al.[27] noted that scoring for the PG-SGA requires training, but the time required for personnel to learn how to use the PG-SGA and to score the first section has not been reported.

Several studies have assessed the validity of the PG-SGA. Persson et al.[26] correlated the PG-SGA scores with serum albumin (S-alb) and pre-albumin (P-alb), and percentage of weight loss and found that PG-SGA scores were significantly associated with S-alb, P-alb, and percentage of weight loss in the last 6 and 12 months. Bauer et al.[22] found that the PG-SGA score was correlated with weight loss in the previous 6 months ($p = 0.012$) and length of hospital stay ($p = 0.06$), but, not with body mass index (BMI). Thoresen et al.[28] found that the PG-SGA score was correlated with percentage weight loss from prediagnosis weight ($p<0.001$), BMI ($p<0.001$), triceps skinfold ($p<0.001$), mid-upper arm muscle circumference ($p<0.001$), S-alb ($p<0.01$), and P-alb ($p<0.001$). Isenring et al.[24] reported that PG-SGA scores correlated with percentage weight loss in the previous 6 months ($p = <0.001$), baseline BMI ($p = 0.008$), quality of life (QOL) at baseline ($p<0.001$), and change in QOL after 4 weeks of radiation therapy ($p<0.001$). Also, survival was significantly higher in patients categorized as "A" compared to "B" or "C" ($p < 0.001$). Finally, Ravasco et al.[4] found that the energy intake (kcal) of cancer patients was associated with PG-SGA scores ($p=0.003$).

Persson et al.[26] evaluated the inter-rater agreement between a physician and dietician and found a 90% inter-rater reliability in the classification of the PG-SGA nutrition categories. Bauer et al.[22] assessed the internal consistency of the seven items of the PG-SGA and found a low Cronbach's reliability coefficient of 0.21. However,

after standardizing for the variance in the distribution of responses, a standardized item alpha coefficient was 0.64.[22]

Bauer et al.[22] also evaluated the sensitivity and specificity of the PG-SGA with 71 in-patient oncology patients on an oncology ward and reported a sensitivity of 98% and a specificity of 82%. The positive predictive value was 95% and the negative predictive value was 93%. Thoresen et al.[28] assessed the sensitivity and specificity of the PG-SGA with 80 in-patient medical oncology patients and reported a sensitivity and specificity of 96% and 83%, respectively. Ravasco et al.[4] also evaluated the sensitivity and specificity of the PG-SGA score with 205 oncology patients in an outpatient radiotherapy department, and reported a sensitivity and specificity of 80% and 89%, respectively. They suggested that the PG-SGA in combination with weight loss over the last 6 months would "…allow the detection of 18% more 'true positive cases', thus increasing its sensitivity and predictive value…" (p 449).[4]

In the initial testing of PG-SGA with 186 oncology patients, Ottery[20] reported that patients triaged as "requiring nutritional intervention," which included symptom management and dietary interventions, had a 50-60% success rate in maintaining weight during antineoplastic therapy. Bauer et al.[22] screened 71 hospitalized oncology patients using the PG-SGA and found that patients triaged as "B" or "C" had increased median length of hospital stay compared to those triaged as "A". Read et al.[27] used the PG-SGA with 157 outpatient oncology patients and found that the number of patients triaged as "requiring nutritional intervention" was reduced by 5% between baseline, 4-6 week, and 8-12 week periods. Horsley et al.[11] evaluated 66 oncology patients prior to peripheral blood stem cell transplantation using the PG-

SGA and found that post-transplant length of stay was 7 days longer for patients triaged as "B" or "C" compared to those triaged as "A".

Overall, the PG-SGA has demonstrated diagnostic value in detecting oncology patients at risk of developing malnutrition or who are malnourished.[22] Patient input not only enhances patient acceptance of the PG-SGA, but also simplifies data collection for the clinician. Evaluation of the mean time required for clinicians to learn how to use the PG-SGA and mean time required to complete nutrition screening would help determine the PG-SGA's practicality. The PG-SGA has been correlated with a number of objective nutrition indicators, as well as quality of life. Additionally, the PG-SGA has a high degree of inter-rater reliability between dieticians and physicians. However, the inter-rater reliability of the PG-SGA between trained nurses and dieticians needs to be evaluated. The high sensitivity and specificity of the PG-SGA suggests that it is a valid method of screening for risk or presence of malnutrition in patients with cancer. Finally, early screening with the PG-SGA directed clinicians to plan for nutrition support which led to improvements in the nutrition status of oncology patients.

2.3.2 *Mini Nutritional Assessment (MNA).*[29] The MNA has been validated for use in elderly subjects (>65 years). However, it has had limited evaluation in the oncology population.[8,27,30-32] The MNA consists of two sections: the first section (A-F) includes screening questions related to weight history, food intake, activity, psychological stress, and body mass index; and the second section (G-R) includes assessment questions related to measurement of arm and calf circumference, specific questions about oral intake and habits, and medical history. A score of < 11 on the first section

suggests that the second section needs to be completed. The summative score on the MNA of < 17 indicates malnutrition, 17-23.5 indicates risk of malnutrition, and ≥ 24 indicates adequate nutrition. The MNA has been translated into more than 15 languages including English, French, Dutch, and Spanish. The MNA takes approximately 10 minutes to complete. Instructions on the use of the MNA are available on the MNA website.[34]

The developers of the MNA suggest that their tool can be easily used by health professionals involved in the care of the elderly. However, because the MNA uses mid-arm and calf circumference measurements to determine nutrition status, training would be required to complete nutrition screening.[17,33] Furthermore, obtaining anthropometric measures from frail or weak oncology patients may be time intensive. Admitting physicians found that the MNA required more time and effort to complete for elderly oncology patients because these patients were quite ill or cognitively impaired.[32] Read et al.[27] noted that the indicators of nutrition status, which included use of more than three medications and number of full meals taken in a day, were problematic in the oncology group because these indictors incorrectly categorized elderly oncology patients as at risk for malnutrition or malnourished. Oncology patients frequently take more than three medications and may have a number of small meals throughout the day to overcome the effects of treatment or early satiety.[27]

Three studies attempted to validate the MNA in elderly cancer patients. Zulian et al.[32] found that BMI, brachial circumference, calf circumference, recent weight loss, mobility, presence of acute disease, and presence of anorexia did not reach levels of significance in elderly cancer patients. Slaviero et al.[8] found the MNA score

correlated with percentage weight change ($p < 0.001$), C-reactive protein ($p < 0.001$), and calf circumference ($p < 0.001$). However, both Read et al.[27] and Slaviero et al.[8] were unable to establish concurrent validity of the MNA with other nutrition screening tools, including the PG-SGA and the Prognostic Inflammatory and Nutritional Index (PINI).

Reliability of the MNA has not been evaluated in the oncology population. However, in a study of hospitalized elderly patients, the inter-rater reliability had a κ of 0.51 (95% CI, 0.28-0.74).[33]

Analysis of the sensitivity and specificity of the MNA against an unintentional weight loss of > 10% over 3 months was 33% and 90%, respectively, [8] and against the PG-SGA was 97% and 54%, respectively.[27] Read et al.[27] measured the positive predictive value of the MNA in 157 oncology patients and reported it to be 59% at baseline assessment, 54% at the 4-6 week follow-up, and 66% at the 8-12 week follow-up.

An advantage to the latest version of the MNA is that it directs clinicians in a plan for nutrition intervention once patients are identified as "at risk" for malnutrition or malnourished. The cost of MNA training has not been documented or evaluated. Furthermore, the benefits of the MNA against clinical outcomes have not been studied in the oncology population.

Overall, the MNA requires further validation and reliability testing in the oncology population. The current diagnostic indicators of the MNA may require modification to be of value in the oncology population. At this time, completing both sections of the MNA is time intensive in elderly oncology patients. Therefore,

modifications to the MNA may be required to improve its practicality for clinicians. Finally, the benefit of the MNA in oncology practice is uncertain because it has not been validated against clinical outcomes in the oncology population.

2.3.3 *Malnutrition Screening Tool (MST).*[35] The MST was originally developed for use in hospitalized acute adult patients.[35] Presently, the MST has only been evaluated in oncology patients undergoing radiation therapy.[36] The MST uses the data obtained from three questions related to weight history and appetite to determine risk of malnutrition. Answers to the questions are scored between 0-5, and a summed score of 2 or more indicates risk of malnutrition. Developers of the MST suggest that patients who are not at risk be re-screened weekly, whereas, patients who are at risk of malnutrition undergo a more detailed nutrition assessment and appropriate nutrition support. Currently, the MST is only available in English.

Developers of the MST suggest that it is simple, quick, and easy to use.[35] Additionally, they suggest that the MST can be completed by health care professionals, administrative staff, family, and patients. However, the time required to complete the MST and its ease of use among medical and nursing staff has not been documented. Additionally, the effectiveness of the MST against clinical outcomes like treatment delays, hospital admissions, and length of hospitalization has not been studied in the oncology population.

Convergent validity was established by comparing the MST score to a SGA score for 106 oncology patients undergoing radiation therapy and according to SGA, 89% of the patients were well nourished and 11% were moderately malnourished; according to the MST, 28% were at risk of malnutrition.[36] Other validity testing has

not been done in the oncology population. In acute care adult patients, the MST was compared to anthropometric (BMI, mid arm circumference, triceps skinfold thickness, midarm muscle circumference, midarm muscle area, and hand grip strength) and biochemical measures (S-alb total protein, P-alb, white cell count, lymphocyte count, c-reactive protein, hemoglobin, and hematocrit)[35] and apart from total lymphocyte count and white cell count, the MST score correlated with the other nutrition indices. Predictive validity was established by comparing the MST to length of hospital stay and patients who were at risk for malnutrition had significantly longer length of hospital stays than those who were not at risk for malnutrition.[35]

Ferguson et al.[35] tested the reliability of the MST between dieticians and found the inter-rater reliability was 96% (κ =0.88, p<0.01). Agreement between dieticians and nutrition assistants on the MST score was 93% (κ =0.084, p<0.01). No inter-rater reliability has been conducted between nurses and dieticians.

The MST has a sensitivity and specificity of 100% and 81%, respectively.[35] The authors suggest that changes to the "cut-off" values for being at risk for malnutrition from 2 to $\geq$ 3 would improve the specificity of the MST to 94%. But these changes would reduce the sensitivity of the MST to 45%. The positive predictive value of the MST was 0.4 and the negative predictive value was1.0.[36]

Overall, the MST is a quick and easy to use screening tool. The MST directs clinicians to a plan for future nutrition care for patients at risk for malnutrition. Since the MST has only been evaluated in cancer patients receiving radiotherapy, further study in other oncology patient populations is warranted before general use in clinical

practice. Finally, the effect of the MST on clinical outcomes in patients with cancer also requires study.

2.4 Conclusion

Malnutrition is a common problem in patients with cancer. Consequently, accurate detection of declining nutrition status is important. Nurses are in an ideal position to carry out nutrition screening of oncology patients. Three nutrition screening tools are recommended for use in oncology patients by the ONS. Of the three recommended tools, the PG-SGA has the most diagnostic value for patients with cancer. The PG-SGA has been validated in both in- and out-patient settings and a variety of oncology patient groups. Additionally, the PG-SGA directs clinicians to a plan of nutrition care and assessment of clinical outcomes. The drawbacks to using the PG-SGA include the time commitment required for training and assessment, and no established inter-rater reliability between dieticians and nurses. The MNA and MST have had limited evaluation in the cancer population. Therefore, further study of these tools is recommended.

Table 2.1

Common Indicators Used to Assess Nutrition Status

Indicator	Use of Information and Limitations
Weight (wt), unintentional wt loss, percentage of wt loss	Wt loss is considered significant when there is a ≥5% in 1month, ≥7.5% in 3 months, 10% in 6 months.
Body Mass Index (BMI)	BMI < 18.5 indicates health risk due to undernutrition, 18.5-24.5 indicates normal range, low risk of illness, ≥25 indicates increased risk for health problems
Serum albumin	≤30 mg/dl indicates protein depletion. Values affected by hydration status, albumin administration, and acute stress. Half life of ~ 20 days.
Serum transferrin	≤150 mg/dl indicates depletion. Values affected by iron deficiency anemia, hemorrhage, dehydration, liver disease, and chronic infection. Half life of ~ 8-10 days.
Serum prealbumin	≤17 mg/dl indicates depletion. Values affected by hydration status, hyperthyroidism, renal failure, and severe liver disease. Half life of 2-3 days.
Retinol-binding protein	≤4.5 mg/dl indicates depletion. Values affected by injury and metabolic stress. Half life ~ 12 hours.
Total lymphocyte count	≤1500/mm^3 indicates malnutrition.
Creatinine: height index	≤60% indicates severe deficiency, and skeletal muscle depletion. Requires accurate 24h urine collection and can be affected by meat intake, renal function, and age.
Skinfold measures – triceps, biceps, subscapular, and suprailliac	Measurements ≤5^{th} percentile is considered an indicator of fat and protein depletion. Variability between assessors.
Bioelectrical impedance	Measurement of fat and fat free mass. Values affected by tumour and fluid status.

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CHAPTER 3 PREDICTORS OF REDUCED FOOD INTAKE, WEIGHT LOSS AND FUNCTIONAL STATUS IN HEAD AND NECK CANCER PATIENTS

3.1 INTRODUCTION

Cachexia is a complex metabolic syndrome associated with underlying illness, whose prominent clinical feature is involuntary weight loss. [1,2] Cachectic cancer patients report markedly reduced quality of life, function and physical ability. The involuntary loss of as little as 5% body weight over six months is associated, with increased treatment toxicities and complications, delayed treatment, lengthened hospital stays and shortened survival.[3]

Weight loss can be attributed to two key components: increased energy expenditure and reduced dietary intake.[4] Normally dietary intake is promoted by physiological, psychological, and social stimuli.[5] Cancer–associated decreases in dietary intake are attributed to a disturbance of appetite control in the hypothalamus.[1,6] Cancer patients state that dietary intake is also compromised by a variety of symptoms (i.e. nausea, vomiting, diarrhea, constipation, taste changes, depression, anxiety, pain) known as nutrition impact symptoms, which constitute barriers to dietary intake,[4,7-10] but there is limited information about the specific contribution of each symptom to reduced dietary intake.

Head and neck cancer (HNC) patients are a uniquely nutritionally vulnerable group because the site of cancer causes additional symptoms such as swallowing difficulty, mouth sores, dry mouth, dental problems, and difficulty chewing, which are also associated with reduced dietary intake.[11,12] Alcohol abuse may compound a nutritional deficit in this patient population.[13,14] Subsequent treatment through surgery, radiation, and chemotherapy impose further nutritional challenges.[11,15]

A number of researchers have reported on the prevalence of nutrition impact symptoms and their relationship to weight loss in patients with HNC. These studies, however, were limited by retrospective designs, variation in the patient subgroups studied, and convenience samples.[16,17] In addition, there was no consensus regarding the symptoms assessed; consequently, symptom prevalence is unclear. But more importantly, these researchers did not evaluate the patient's actual dietary intake. Thus, there is no clear picture of the relationships, if any, between nutritional impact symptoms, reduced dietary intake or weight loss. The accurate determination of the type and number of symptoms perceived by patients to influence dietary intake prior to treatment may identify patients at greatest risk for reductions in dietary intake, weight loss, functional capacity during treatment, and survival. The study described in this paper used the Patient Generated-Subjective Global Assessment (PG-SGA)[18] to systematically collect information on symptoms known to affect dietary intake, as well as on dietary intake, weight loss, and functional capacity.

Our primary objective was to describe the prevalence of symptoms known to influence dietary intake in patients with HNC prior to treatment, and to investigate the relationship between these symptoms and dietary intake, weight and functional capacity. Survival analysis is not included since only 21% of the sample is deceased. Participants in this study will be followed for 5 years, and survival analysis will be completed at that time.

3.2 Materials and Methods

This study was approved by the Research Ethics Committee of the Alberta Cancer Board. A computerized database of all cancer cases in Alberta (Cancer Registry) codes primary cancers by their site and morphology, and also provides biological, clinical, and demographic information. This source was used to confirm clinical and demographic information, as well as the proportion of total cases evaluated during the study period. Since data were collected as part of standard care, our goal was to recruit all adult HNC patients in the region referred for consideration of surgery, radiation and or chemotherapy were included.

We adopted a population – based approach to examine the nutritional features of HNC patients. According to the Alberta Cancer Registry, there were approximately 430 new cases per year of HNC during the time period covered by this study. Since data gathering did not begin until August 2004, we estimate that our sample represents 80% of the individuals living in northern Alberta (population 1.8 million) who were diagnosed during the study period. Newly diagnosed patients with HNC were screened using the PG-SGA as part of routine clinical care, prior to treatment.

The PG-SGA is a validated nutrition screening tool designed specifically for patients with cancer.[18-20] The scored section of the PG-SGA was used to evaluate weight loss history, which is scored as follows:

Grade	%Weight Loss in 1 month	% Weight loss in 6 months
0	0-1.9 %	0-1.9 %
1	2-2.9 %	2-5.9 %
2	3-4.9 %	6-9.9 %
3	5 -9.9 %	10-19.9 %
4	≥ 10 %	≥ 20 %

In addition to reported weight loss, the PG-SGA provides information about height, dietary intake, 14 symptoms that interfere with dietary intake, and functional capacity. The functional capacity component of the PG-SGA is a lay version of the Eastern Cooperative Oncology Group (ECOG) performance status score.

For the purposes of this study the total number of symptoms reported by each patient was considered to be a continuous variable and all other variables were considered dichotomous as follows: weight losses in 6 months (Grade 0 or ≥ Grade 1), dietary intake (normal or reduced), symptoms (present or absent), and functional capacity (normal or reduced). Since a number of research groups have shown that 5% weight loss in 6 months is associated with adverse patient outcomes, we were primarily interested in the differences in study variables between individuals with Grade 0 and Grade 1 weight loss.[21-23]

3.2.1 *Data Analyses*

Descriptive statistics were used to describe the frequency of symptoms, Body Mass Index (BMI) category, dietary intake, and functional capacity. Independent t-tests (2-tailed) were used to compare patients with Grade 0 weight loss to those with ≥ Grade 1 weight loss on the total number of symptoms, dietary intake, weight loss, and tumour stage. Spearman's correlations were calculated to assess bivariate associations between weight loss and each of the potential independent variables. Univariate logistic regression was used to detect an association between individual symptoms and each of the three independent variables (dietary intake, weight loss, and functional capacity). The variables found to be significantly associated with reduced dietary intake, weight loss or reduced functional capacity in the univariate

analyses were then entered into a multivariable logistic regression model using a hierarchical data selection method to construct a final model. We then constructed hierarchical models in which we considered each of the variables after retaining all significant variables from the previous step[23,24] A *P* value of <0.05 was considered statistically significant. A Cumulative hazards model was conducted on symptoms to determine time to event (5% weight loss).[25]

3.3 Results

3.3.1 *Patient Demographics*

Between August 2004 and February 2007, n=350 patients were evaluated. Characteristics of the patients are shown (Table 3.1). Data are presented as group means ± SE. No gender-based differences were detected in any variable and thus values for males and females were pooled.

3.3.2 *Nutrition Symptoms and Weight Status*

Prior to treatment, 37% of the patients experienced none of the 14 nutrition impact symptoms, but the remaining 63% recorded a total number of 629 symptoms (1-10 per patient). One or more symptoms were reported more commonly by patients with localized tumours to the pharynx (72%), paranasal sinuses and oral cavity (68 %), and the larynx (57%) compared to those with tumors of the salivary gland (40%) or thyroid (33%). On average fewer total symptoms were experienced by patients staged as T1/T2 (1.3 ± 0.18 symptoms), than T3/T4 patients (2.4 ± 0.12 symptoms; p< 0.0001). A reduced dietary intake during the preceding month was reported by 61% of patients, and these experienced a greater number of symptoms (2.4± 0.15 symptoms), than those with normal dietary intake (0.76 ± 0.10; p< 0.0001). There

was a moderate but significant correlation between the total number of symptoms and reduced dietary intake (r=0.448, p< 0.0001).

The mean BMI of the patient group was 26.2 kg/m^2 ± 5.29 (median 25.7; range 14.7 to 53.2). By World Health Organization (WHO) standards, 32% of patients had normal BMI (18.5 to 24.9 kg/m^2) and 57% were overweight or obese (Figure 3.1A). The percentage of patients with BMI < 18.5 (10%) was relatively small, and they were more likely to be >65 years of age and to have pharyngeal or oral cavity tumours.

Overall, the history of weight loss reported by patients at presentation was modest, but this value had a large standard deviation. The weight loss quartiles (Figure 3.1B) revealed considerable heterogeneity. Quartiles 3 and 4 (182/350) had been weight stable over the preceding 6 months, or had gained a small amount over this time (39/350). Quartiles 3 and 4 had an average BMI of 27.2 (± 5.2), with only 4% having a BMI <20. Quartiles 1 and 2 were weight losing (n=168) and had an average BMI of 25.2 (± 5.1), of these 17% had a BMI <20.

The patients with the most significant history of weight loss were more likely to have tumours of the pharynx and oral cavity. On average more symptoms were reported by patients with Grade 1(2.68 ± 0.20), than those with Grade 0 weight loss (1.4 ± 0.12; p < 0.0001). There was a weak but significant correlation between the total number of symptoms and Grade 1 weight loss (r=0.337, p < 0.0001).

3.3.3 *Nutrition Impact Symptoms Predictive of Reduced Dietary Intake, Weight Loss, and Reduced Functional Capacity*

Table 3.2 shows the frequency of nutrition impact symptoms. Pain and problem swallowing were the most common symptoms; these and other symptoms such as no appetite, sore mouth, taste changes, dental problems, dry mouth, and other (depression, no money) were prominent in patients with a reduced dietary intake, with Grade 1 weight loss, as well as in patients exhibiting a reduced functional capacity.

Overall 47% of patients rated their functional capacity as reduced. On average more symptoms were reported by patients with reduced functional capacity (2.7 ± 0.01), than those patients with normal functional capacity (0.91 ± 0.10; $p < 0.0001$). Also a significantly greater number of patients with reduced functional capacity experienced Grade 1 weight loss compared to those with normal functional capacity ($p<0.0001$). There was a moderate but significant correlation between the total number of symptoms and reduced functional capacity ($r=0.485$, $p < 0.0001$).

A hierarchical multivariate logistic regression was conducted to identify the nutrition impact symptoms that significantly predicted dietary intake, Grade 1 weight loss, and reduced functional capacity (Table 3.3). No appetite, problem swallowing, pain, and taste changes were significant predictors of reduced dietary intake. This final model as a whole explained between 17.8% (Cox and Snell R^2) and 24.2% (Nagelkerke R^2) of the variance in reduced dietary intake, and correctly classified 69.4% of the cases. No appetite, problem swallowing, and pain were significant predictors of Grade 1 weight loss. This final model as a whole explained between

16.7% (Cox and Snell R^2) and 22.7 % (Nagelkerke R^2) of the variance in Grade 1 weight loss, and correctly classified 68.4% of the cases. No appetite, problem swallowing, feeling full, and pain were significant predictors of reduced function capacity. This final model as a whole explained between 26.1% (Cox and Snell R^2) and 34.8% (Nagelkerke R^2) of the variance in reduced function capacity, and correctly classified 73.7 % of the cases.

The Cumulative Hazard statistics for days to 5% weight loss for patients with presence or absence of no appetite, problem swallowing, and pain (each statistically significant multivariate nutrition impact symptom) is shown (Figure 3.2A). The mean number of days to 5% weight loss for patients reporting problems swallowing was 116 days (SE = 6.5; 95%CI = 104 to129) vs. those patients with no problem swallowing was 156 days (SE = 3.1; 95%CI = 150 to 162); for patients reporting pain was 127 days (SE = 6.0; 95%CI = 116 to 139) vs. those patients with no pain 153 days (SE = 3.4; 95%CI = 146 to160); and for patients reporting no appetite 121 days (SE = 9.3; 95%CI = 103 to139) vs. for patients with appetite 149 days (SE = 3.2; 95%CI = 142 to 155). The Cumulative Hazard statistics of days to 5% weight loss stratified by total number of significant multivariate symptoms (loss of appetite, pain, problems swallowing) for HNC patients is shown (Figure 3.2B). The mean days to 5% weight loss for patients with HNC reporting no symptoms impacting dietary intake was 165 days (SE = 3.1, 95%CI = 159 to 171) vs. those patients reporting one symptom was 140 days (SE = 6.0; 95%CI = 128 to 151) vs. two symptoms was 105 days (SE = 8.6; 95% CI = 87 to 122) vs. three symptoms was 97 days (SE = 15.0; 95% CI = 67 to 125).

3.4 Discussion

In our population-based study using – the PG-SGA to evaluate the nutritional features of HNC patients prior to treatment, we found that prior to treatment, HNC patients are strikingly heterogeneous with respect to weight, weight loss history and a variety of symptoms affecting dietary intake. Further, while a certain proportion is clearly well nourished, others exhibit important signs of malnutrition. Although problems swallowing is generally regarded as a principal cause of reduced dietary intake and weight loss our results suggest, several other symptoms (pain, loss of appetite, and chemosensory dysfunction) associate independently and strongly with reduced dietary intake as well as with weight loss and reduced functional capacity.

Our results suggest that although individuals with HNC, appear generally well nourished prior to treatment, there are several reasons why this may not be the case. Like many contemporary cancer patients, our HNC cohort were more likely to be overweight or obese (ie ~60% of patients) than underweight (<10%) at presentation. Only a small fraction (15%) of the patients had a history of Grade 3 or Grade 4 weight loss, which is similar to that reported by Jager-Wittenaar et al. (2007).[17] A high body weight may mask concurrent loss of lean body mass and we have recently shown that in obese patients with solid tumors depletion of the lean body mass was associated with poorer functional capacity ($p=0.009$), and was an independent predictor of survival (HR = 4.2, $p<0{\cdot}0001$; 95% CI 2.4 to 7.2).[26] Based on these findings we suggest that assessment of lean body mass is an essential component of nutritional assessments of cancer patients. A HNC patient's pre-treatment body weight must be framed against the further losses expected during

treatment. With radiotherapy alone, treatment – related losses may be in the order of 5% of body weight, but combined with other adjuvant treatments may provoke further losses in the range of 15-20%.[23, 27-29] In the context of the significant risks of both pre-treatment and post-treatment weight losses, a large body weight is an advantage; higher body mass index was significantly associated with longer survival in HNC patients (HR, 0.54; 95% CI 0.39 to 0.74).[30] It follows from this that what is considered the normal body weight range for adults (BMI 18.5-24.9) may be too low for patients expecting to sustain large losses during treatment.

In our study, we found that HNC patients who presented with multiple symptoms prior to treatment were more likely to have reduced dietary intake, weight loss, and reduced functional capacity. Generally, little attention is paid to the systematic assessment and management of symptoms in HNC patients prior to treatment.[16,17] It could be argued that evaluating and managing these symptoms pre-treatment is rather futile since they are also an inevitable part of treatment, and will likely resolve once treatment is completed. This argument however, demonstrates a lack of general knowledge about the relationship between these symptoms and reduced dietary intake, involuntary weight loss, and functional capacity. The onset of any **one** symptom may reduce dietary intake, but the accrual of multiple symptoms may hasten weight loss, which is borne out by our results (see Figure 3.2B). Furthermore, a high symptom burden has been reported to influence functional capacity.[31-33] If symptoms that influence dietary intake are not assessed and managed early in the treatment plan, it is unlikely that involuntary weight loss can be prevented.

This study specifically investigated symptoms that had a direct impact on dietary intake. Pain, loss of appetite, and taste changes, were all found to be factors associating significantly with reduced dietary intake independently of problem swallowing. Our findings suggest that symptoms other than problem swallowing are involved with involuntary weight loss in patients with HNC, and this realization may be critical to the development of therapeutic interventions.

Not surprisingly, **problem swallowing** was prevalent and highly associated with reduced dietary intake, weight loss and reduced functional status. Patients who experienced difficulty swallowing lost 5% body weight 40 days earlier than those without swallowing difficulty. Problems swallowing may remain unresolved even six months to one year after treatment resulting in persistently low food intake and weight loss.[34-36] Evaluation and management of this critical function during treatment may improve dietary intake, functional capacity, and reduce weight loss.

Loss of appetite was also an important independent predictor of low intake, weight loss, and reduced functional capacity. Loss of appetite is a common symptom in patients with solid tumours. [1,4,6] The etiology of cancer anorexia is partially understood. It has been suggested that cancer anorexia results from the secretion of pro-inflammatory cytokines such as tumour necrosis factor, interleukin-6 and interleukin-8 acting as anorexigenic agents resulting in reduced dietary intake.[37-39] Additionally, disruptions in the signaling pathways of neuropetides such as leptin, ghrelin, and neuropeptide Y are proposed.[38,40] Anorexia is the target for a variety of orexigenic therapies such as dexamethasone and progestational agents. This is an area of intensive investigation, with agents such as ghrelin, CB1 receptor

(cannabinoid) agonists and melanocortin receptor modifiers currently in development or in early clinical trials. These results suggest that examining the drivers for the loss of appetite of HNC patients should be the subject of future investigations.

Pain is a common complaint of patients with HNC.[41-43] Pain has been reported to compromise spontaneous food intake in patients with advanced cancer.[44,45] Additionally, pain has been strongly associated with reduced functional capacity.[31,32] The physiological effects of pain stimulate the stress response which increases catabolism and stimulates the release of catecholamines that alter gastrointestinal activity.[5] Control of pain and other distressing symptoms improved elderly terminal cancer patient's and advanced cancer patients dietary intake, as it allowed patients to be receptive to having food, even when experiencing little or no appetite.[44,45] Thus, it is conceivable that with improved pain control before the onset of treatment, spontaneous dietary intake could be improved.

Taste changes are usually considered sequelae of RT and chemotherapy, [46] yet we found 25% of patients with weight loss reported this as a symptom which prevented them from eating prior to treatment. We recently found that advanced cancer patients with solid tumours who had severe taste and smell complaints had low dietary intake, elevated rates of weight loss and lower quality of life compared to patients who had no or mild alterations in taste and smell.[47]

There was a limitation in this current study. Cancers of the thyroid are not usually included in the category of head and neck cancers. Patients with cancer to the thyroid do not typically report the same nutrition impact symptoms as those patients

with head and neck cancers. However, the thyroid patients who were included in the study had tumours which had invaded adjacent structures lying within the neck region and their number was small (nine). Therefore, it is unlikely that their inclusion would have changed our results.

This study underscores the value of adopting a nutritional screening tool like the PG-SGA for a new patient clinic of HNC patients. First, it enables clinicians to consider current weight and past weight losses of HNC patient in light of future expected weight losses during treatment. Second, it enables clinicians to frame involuntary weight loss within the context of the patient's dietary intake. Finally, it enables clinicians to evaluate **all** potentially treatable symptoms of the HNC patient contributing to reduced dietary intake prior to the onset of any treatment.

We have demonstrated that symptoms may play a role in reducing dietary intake of HNC patients. Further study of these symptoms before, during, and after oncology treatment may aid in the understanding the underlying causes to reduce dietary intake, weight loss, and reduced functional capacity.

Table 3.1 Demographic profile of Head and Neck Cancer Patients (n=350) at presentation

Patient characteristics	
Gender, number (%)	
Male	248 (70)
Female	102 (30)
Age (years)	
Mean	61
Range	23-92
> 50	285 (81)
> 65	142 (41)
Tumour localization,[a] number (%)	
Oral cavity	104 (29)
Salivary gland	20 (6)
Paranasal sinuses	8 (2)
Pharynx	112 (32)
Larynx	64 (18)
Thyroid	9 (3)
Other[b]	33 (9)
Tumour Stage, number (%)	
Tx – minimal requirement	15 (4)
Tis – carcinoma in situ	5 (1)
T1	74 (21)
T2	92 (26)
T3	52 (15)
T4	94 (27)
Not reported	18 (5)

[a] as per ICD defined codes- for head and neck cancer

[b] unknown primary site

Table 3.2 Prevalence of nutrition impact symptoms of all Head and Neck Cancer Patients at presentation and stratified by those patients with reduced dietary intake, grade 1 weight loss, and reduced functional capacity

Nutrition Impact Symptom	All Patients (%) n=350	Reduced Dietary Intake[a] (%) n= 214	Grade 1 Weight Loss[b] (%) n=168	Reduced Functional Capacity[c] (%) n=163
Loss of Appetite	15	22	25	28
Pain	32	41	41	45
Problem Swallowing	29	37	43	48
Sore Mouth	17	22	21	22
Dental Problems	17	21	20	25
Dry Mouth	15	20	20	23
Taste Changes	10	15	15	15
Feeling Full	9	15	13	17
Constipation	10	13	14	18
Nausea	4	6	5	6
Altered Smells	3	4	5	7
Diarrhea	3	4	3	4
Vomiting	2	3	2	4
Other (depression, no money)	16	21	22	20

[a] from dietary intake component of the PG-SGA
[b] from weight history component of the PG-SGA
[c] from functional component of the PG-SGA

Table 3.3 Univariate and multivariate logistic regression analysis of nutrition impact symptoms, reduced diet intake, grade 1 weight loss, and reduced functional capacity for Head and Neck Cancer Patients at presentation

	Univariate Logistic Analysis			Multivariate Logistic Analysis		
Nutrition Impact Symptom	Reduced Dietary Intake Odds ratio (CI-95%)	Grade 1 Weight Loss Odds ratio (CI-95%)	Reduced Functional Capacity Odds ratio (CI-95%)	Reduced Dietary Intake Odds ratio (CI-95%)	Grade 1 Weight Loss Odds ratio (CI-95%)	Reduced Functional Capacity Odds ratio (CI-95%)
Loss of Appetite	19.3* (4.6-81.1)	7.2* (3.2-15.9)	13.8* (5.3-35.9)	14.2* (3.3-60.0)	5.6* (2.4-12.6)	9.3* (3.4-25.5)
Problem Swallowing	3.0* (1.8-5.2)	3.8* (2.3-6.2)	5.8* (3.4-9.7)	1.9† (1.1-3.5)	2.8* (1.6-4.8)	4.0* (2.2-7.0)
Pain	3.4* (2.0-5.9)	2.2* (1.4-3.5)	3.2* (2.0-5.2)	2.5* (1.4-4.5)	1.6† (1.0-4.6)	2.1* (1.2-3.7)
Taste Changes	5.5* (1.9-16.2)	3.0* (1.3-6.4)	2.7* (1.3-5.8)	3.0† (1.0-9.5)		
Feeling Full	1.2 (0)	2.8‡ (1.2-6.4)	12.7* (3.7-42.7)			5.7* (1.5-0.9)
Nausea	8.0‡ (1.0-62.3)	1.7 (0.5-5.5)	4.0† (1.0-4.8)			
Constipation	2.7‡ (1.1-6.5)	2.2‡ (1.0-4.6)	6.5* (2.6-16.1)			
Sore Mouth	3.1* (1.5-6.4)	1.9‡ (1.1-3.5)	1.9† (1.0-3.4)			
Smells Bothersome	2.9 (0.6-13.8)	2.9 (0.7-11.4)	1.3 (0)			
Dental Problems	2.8* (1.4-5.5)	1.8† (1.0-3.2)	3.0* (1.6-5.5)			
Dry Mouth	2.8* (1.8-8.8)	2.4* (1.3-4.6)	3.6* (1.8-6.9)			
Other (depression, no money)	3.3* (1.6-6.9)	2.5* (1.4-4.7)	1.7 (0.9-3.1)			

* $p<0.001$, † $p<0.05$, ‡ $p<0.01$

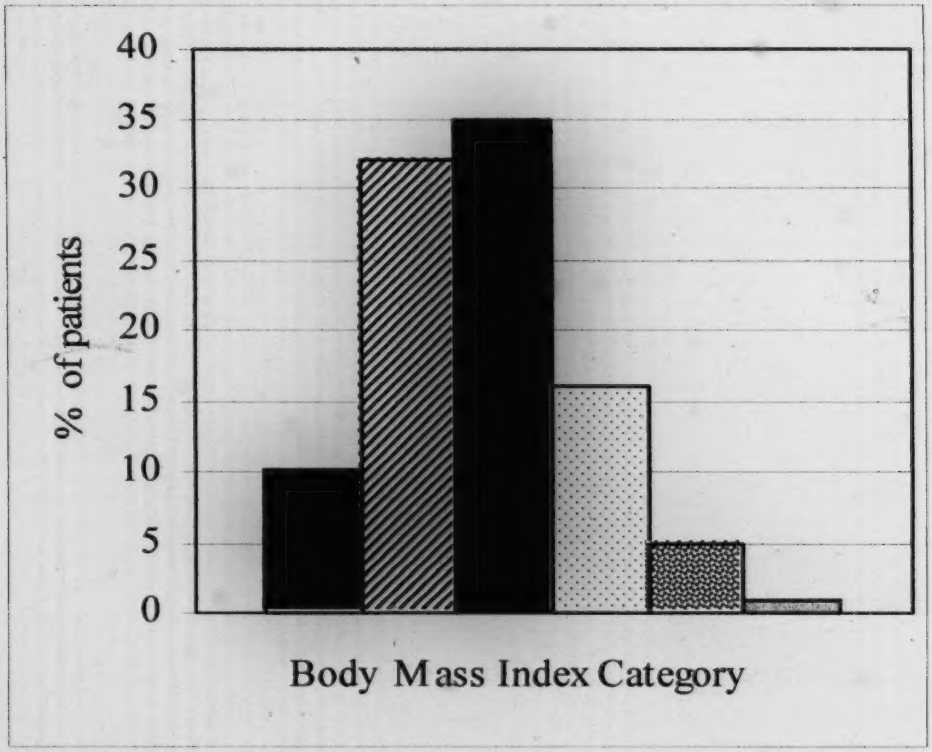

Figure 3.1a. Distribution of body mass index category (in percentage) in head and neck cancer patient population.

Patient distribution of body mass index (BMI) category at time of assessment; underweight < 18.5 ; normal weight 18.5-24.9 ; overweight ≥ 25-29.9 ; class I obesity ≥ 30-34.9 ; class II obesity ≥ 35-39.9 ; ≥ 40 .

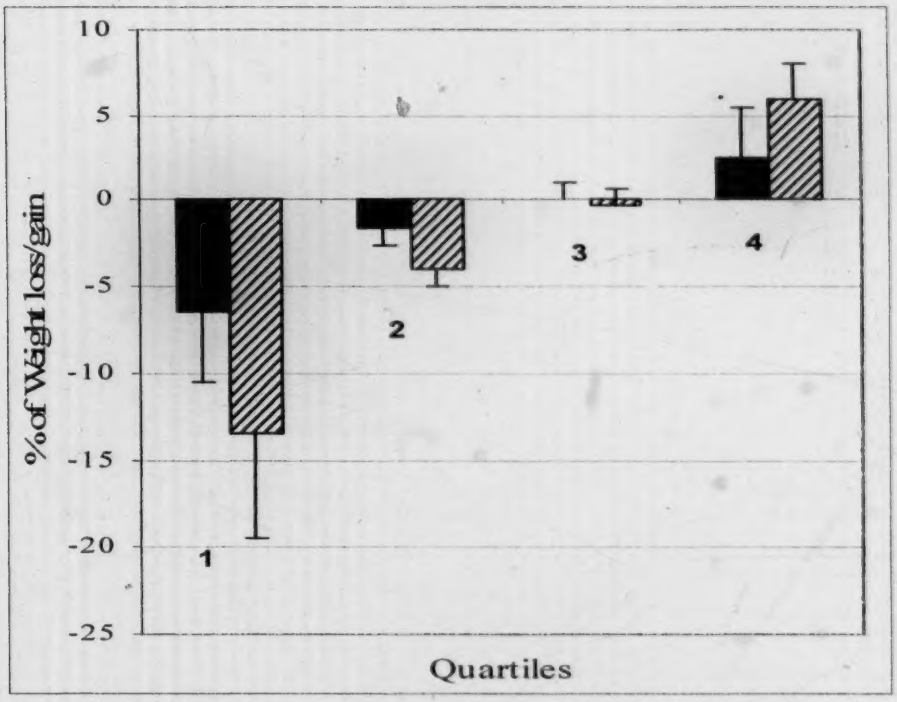

Figure 3.1b. Weight change history of head and neck cancer patient population, by quartiles
Patient reported weight history over the 1 month (■) and 6 months (▨) preceding date of assessment. Mean values for history of weight loss showed high variability (Mean body weight loss over 1 month -1.50 ± 4.03 and over 6 months -3.13 ± 7.30. Population quartiles illustrate the presence of weight stability, loss and gain in distinct quartiles.

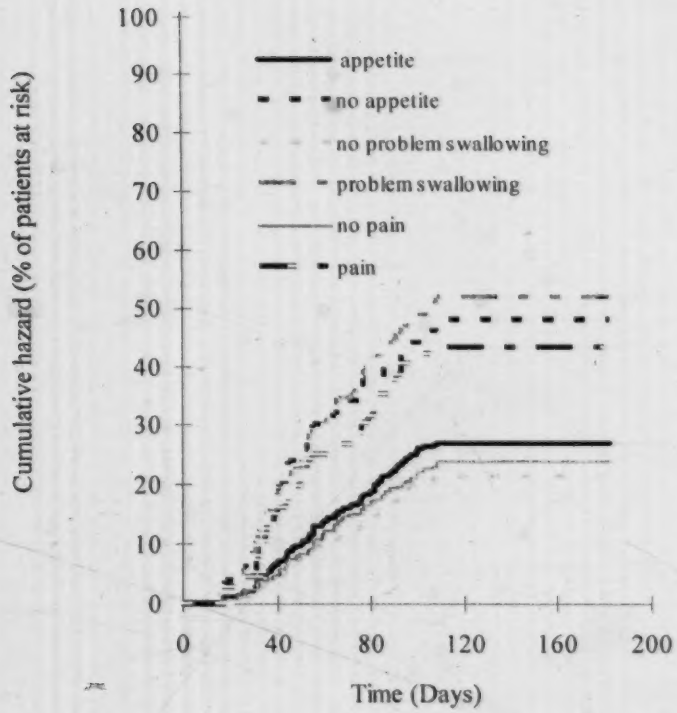

Figure 3.2a. The cumulative hazard statistic of days to 5% weight loss in head and neck cancer patients with and without symptoms. Loss of appetite, problem swallowing, and pain were symptoms identified as statistically significant associates of Grade 1 weight loss in multivariate analysis.

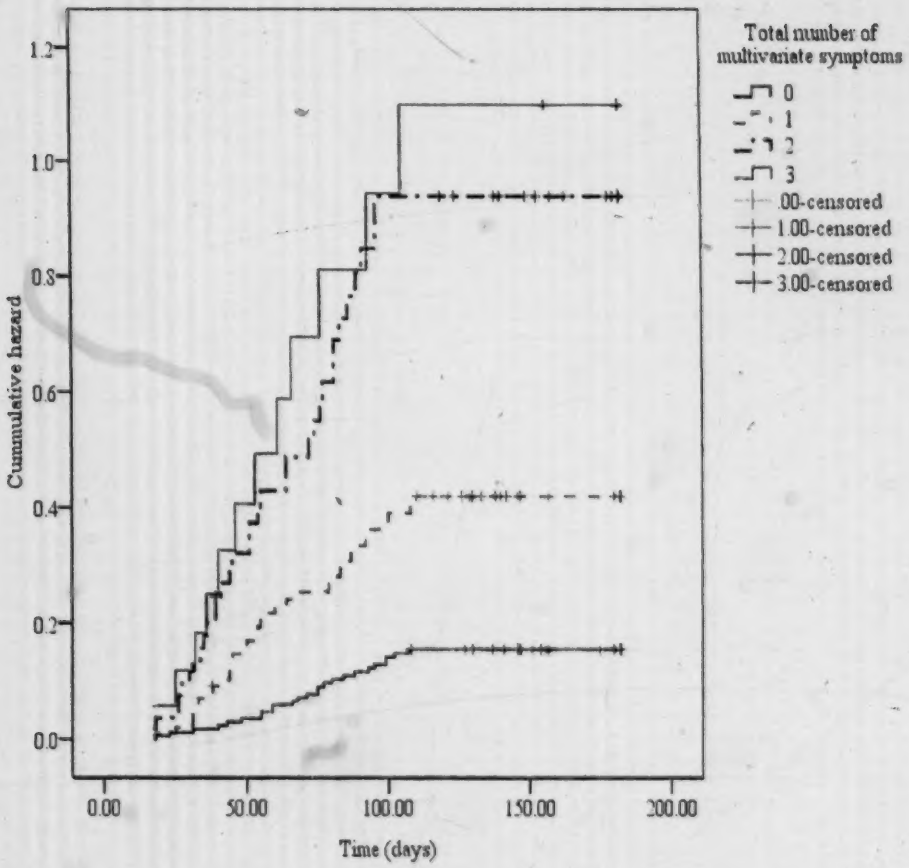

Figure 3.2b. Cumulative hazard statistics of days to 5% weight loss, stratified by the total number of symptoms (0, 1, 2, or 3 of (loss of appetite, problem swallowing, and pain) in patients with head and neck cancer.

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CHAPTER 4 LONGITUDINAL VIEW OF ENERGY INTAKE, WEIGHT LOSS, PERFORMANCE STATUS, AND QUALITY OF LIFE IN PATIENTS BEING TREATED FOR CANCER OF THE HEAD AND NECK

4.1 INTRODUCTION

Head and neck cancer (HNC) accounts for 5% to 6% of all cancers diagnosed in Canada per year, with 4,331 new cases and 1513 deaths reported in 2004.[1] In the past radiotherapy (RT) was the standard treatment for HNC but in the last decade, RT has been combined with other treatments including surgery and /or chemotherapy. Although, the addition of these treatments has improved tumour control rates and survival for HNC,[2-4] it has also increased weight loss and symptom acuity.

Weight loss is associated with increased treatment toxicities and complications, treatment delays, lengthened hospital stays, and is an independent predictor of mortality, especially in patients with stage III and IV tumours.[5-8] Also, weight loss may result in overwhelming fatigue, and markedly reduced functional capacity and quality of life (QOL). Weight loss is generally attributed to an energy imbalance, either an increase in energy expenditure from altered metabolic rate or decreased energy intake from reduced dietary intake, or both.[9-11] Only limited information is currently available on the degree of weight loss and energy intake in relation to various treatment strategies over the time period of diagnosis to follow-up in HNC patients. While preventing weight loss may seem straightforward, efforts to prevent weight loss with oral liquid nutrition supplements or with orexigenic agents have limited success in attenuating weight loss.[12-15]

Tumour presence and cancer treatments may alter energy expenditure in cancer patients. In cancer patients, acute phase inflammatory response proteins including C-

reactive protein (CRP) have been positively associated with weight loss and increased energy expenditure.[16,17] HNC cell lines produce acute phase inflammatory response proteins and elevated concentration of these proteins have been found in most HNC patients.[18-20] Weight loss during treatment for HNC is a well known occurrence.[21-23] However, few studies have prospectively studied the effects of treatment on acute phase inflammatory response proteins like CRP in HNC patients.[24] HNC patients' weight loss may in part be related to systemic inflammation and may contribute to weight loss in patients with HNC.

Additionally, HNC patients' weight loss may be explained in part by the alterations in dietary intake. Our impetus to eat is influenced by physiological, psychological, and social stimuli.[25,26] In cancer patients, decreases in dietary intake are attributed to disturbances of appetite control in the hypothalamus.[9,10,27] Researchers have also reported that certain symptoms including nausea, vomiting, diarrhea, constipation, taste changes, depression, anxiety, and pain may interfere with the stimuli that promote dietary intake.[28-30]

HNC patients commonly experience a myriad of symptoms during treatment. Symptoms including anorexia, nausea, vomiting, mucositis, xerostomia, dysphagia, and chemosensory changes may affect the impetus to eat and increase the risk of reduced dietary intake in HNC patients. Furthermore, while some symptoms are reported to be transient others may continue to be experienced up to one year after treatment.[31-35] Thus, evaluating the symptoms that reduce dietary intake, may explain some of the involuntary weight loss in HNC patients. Currently, the impact of these symptoms on dietary intake and involuntary weight loss over time has not been

explored. Knowledge of mediators that alter metabolism and the symptoms that reduce dietary intake over time in HNC patients may be helpful in designing interventions that prevent involuntary weight loss and improve survival outcomes.

In the current study, we analyzed the patterns of dietary intake, weight loss, functional performance, and quality of life experienced by HNC patients. We also evaluated the potential consequences of systemic inflammation and a series of symptoms known to be common in individuals with HNC on weight, dietary intake, functional performance, and quality of life (QOL) of patients with HNC over time. The primary purpose of this study was to examine relationships between swallowing ability, xerostomia, mucositis, taste and smell function, loss of appetite, and pain and weight, dietary intake, functional performance, and QOL at three points in time—pre-treatment, last day of treatment, and at follow-up, and to evaluate changes between these relationships over time.

We hypothesized that the systemic inflammation and symptoms associated with the addition of chemotherapy to other forms of treatment for HNC result in significant declines in dietary intake, weight loss, functional performance, and QOL in HNC patients compared to patients who do not receive chemotherapy.

4.2 Materials and Methods

The study was approved the by the Research Ethics Committee of the Alberta Cancer Board and the Health Ethics Review Board of the University of Alberta. All patients were >18 years old, spoke English, and signed a written informed consent prior to enrollment.

For the purposes of this study, sample size calculations[36] were based on participants' weight at baseline using the results of Lee (1999) and Silver et al. (2007) where $m=(2*(Z_\alpha + Z_\beta)^2\{1+(n-1)\rho\}) / (n*\Delta^2)$, and m is the number of patients per group, Z_α is the standard normal deviate for a type I error (1.96), Z_β is the standard normal deviate for type II error (0.84), n is the number of time points over which data were collected, and ρ is the intertemporal correlation between scores.[22,24] For the purposes of this study, rho was set at 0.60 . The Δ was calculated by dividing d (the difference between the mean weights at baseline for the chemo and no chemo groups) by the smallest meaningful difference in standard deviation units for the chemo group (effect size) if $\alpha=0.05$, power $(1-\beta)=0.8$ using the weights the weight's provided by Lee (1999) and Silver et al. (2007).[22, 24] Taking this approach, d=15.57 and $\sigma=15.32$, and the required sample size per groups (chemotherapy and no chemotherapy) was 11 patients. Because the rate of attrition and potential requirements for artificial feeding were unknown, recruitment continued until a minimum of 11 evaluable cases in the chemo and no chemo groups were accrued. Thus, fifty-nine HNC patients were prospectively enrolled in this study before they received treatment with curative intent at the New Patients Clinic of the Cross Cancer Institute. Data were collected at three time points –first clinic visit (T1), within three to 5 days of completion of the radiation treatment (T2), and approximately eight to twelve weeks after completion of treatment (T3). (see Figure 4.1) For the purposes of this study these time points (treatment periods) have been labeled T1, T2, and T3, respectively. Of those 59 patients, 2 patients withdrew after baseline recordings, 4 patients died after initial assessments, 9 patients were withdrawn as they did not complete treatment, and

another 6 patients were withdrawn as they received enteral tube-feeding during T2 and T3. The results reported here are based on the remaining 38 patients.

All patients in this study received RT, often in combination with some other treatment. Patients were treated according to standard protocols depending on stage, location, and general health conditions and thus received radiotherapy only (RT), surgery followed by radiotherapy (surgery RT), concomitant radiotherapy and chemotherapy (RTchemotherapy), or surgery followed by concomitant radiotherapy and chemotherapy (surgery RTchemotherapy). The total RT doses ranged from 66-77Gy in daily factions of 1.8 to 2.0 Gy. The treatment protocols for chemotherapy included either carboplatin or cisplatin and 5-fluorouracil.

Height and Body Weight. Patients' body weight was measured with light clothes and without shoes using a calibrated digital platform scale, and recorded to the nearest 0.1 kg, and height was measured on a stadiometer and recorded to the nearest 0.1cm. History of weight loss over the previous one month and six months was self-reported at time of diagnosis. Weight loss was assessed by calculating the percentage weight loss in comparison with the patient's self reported body weight one month prior to diagnosis.

Dietary Intake. Dietary records detailing intake for three consecutive days were used to assess patients' energy intakes. This approach has been reported to be a valid and reliable estimate of current dietary intake.[37,38] A nurse instructed patients on the completion of the dietary record and reviewed the records with each patient to ensure accuracy and completeness. Dietary records were completed prior to treatment, 3 days before T2, and 3 days before T3.

The three day dietary records were entered into the Food Processor II Nutrient Analysis Program™ (Esha Research, Salem, OR), using the Canadian Nutrient File Database Analysis to estimate mean energy and protein intakes. Mean energy intakes were expressed in kcal/day (kcal/d) and kcal/kg body weight (BW)/day (kcal/kg/d). Protein intakes were expressed in gm/day. The European Society for Clinical Nutrition and Metabolism (ESPEN) currently recommends for ambulant cancer patients a mean energy intake between 30 – 35 kcal/kg/d and mean protein intake between 1.2-2g/kg/d.[39]

Functional Performance. A lay version of the Eastern Cooperative Oncology Group (ECOG) functional performance score was adopted to evaluate functional performance. Patients scored their functional performance from 0-3; higher scores indicated poorer functional performance.

Quality of Life. Quality of life was assessed using the University of Washington Quality of Life revised questionnaire (UWQOL).[40] This instrument was developed and validated to measure the quality of life of patients with HNC. Patients rated the following domains: pain, appearance, activity, recreation, taste, chewing, speech, swallowing, saliva, and shoulder disability. Each domain was scored from 0 to100. A cumulative UWQOL score was calculated by summing the scores from each of the 10 domains (0 to1000); higher scores indicate better quality of life.

Systemic Inflammation. (CRP). Venous blood samples were collected from patients at the Cross Cancer Institute in vacutainer tubes for determination of CRP. Serum CRP concentrations were measured using an automated immuno-turbidmetric assay

within the Alberta Provincial Laboratory. Serum CRP concentrations of ≥10mg/l indicate the presence of systemic inflammation.[41]

Nutrition Impact Symptoms

Loss of Appetite or Pain. Patients were asked "Has this symptom interfered with your eating?". Patients then rated their loss of appetite or pain using a 5- point Likert scale. The scoring ranged from "1=not at all" to "5= a lot", with a neutral point at "3=somewhat". Higher scores on the symptom scale denoted greater interference with eating. A loss of appetite or pain score of ≥3 is considered clinically significant.

Swallowing Capacity. The researchers adopted the timed test of swallowing developed and validated by Nathadwarawal et al. (1992).[42] Each patient was comfortably seated and the test was explained. Patients were first observed during intake of 10 ml of tap water in a standard glass to determine risk of dysphagia. Patients who choked, sputtered, or had a wet hoarse voice after drinking 10 ml of water did not complete the second part of the timed swallowing test. Patients who successfully complete the first drinking test were then given 90 ml of tap water in a standard glass. The throat area was exposed to allow the number of swallows to be counted by noting movements of the thyroid cartilage. Sitting to one side, a nurse asked the patient to place the glass to the lips but not to start drinking until the "go" signal. The patient was instructed to drink all the water, as fast as possible, but safely, and to stop if they experienced any discomfort. If the patient could not drink the whole amount, the residual volume was measured. The time from the "go" signal to the end of the last swallow indicated by return of the thyroid cartilage to its resting position was measured with a stopwatch; the number of swallows was counted. The

swallowing speed (ml/sec) was calculated. A swallowing speed of ≤10ml/sec is considered clinically significant.[42]

Oral Mucositis Grade. The revised Western Consortium of Cancer Nursing Research Stomatitis Staging System (WCCNR-SSS) was adopted to assess oral mucositis.[43] The presence and severity of oral lesions, colouring of the oral mucosa, and presence and severity of bleeding were each scored from 0-3, respectively. A cumulative score (0-9) was calculated by summing the scores from the lesion, colour, and bleeding scores. Higher scores denoted worsening oral mucositis. An oral mucositis score ≥5 is considered clinically significant.[43]

Xerostomia Grade. The Common Terminology Criteria for Adverse Events (CTCAE), version 3.0, of the National Cancer Institute of xerostomia grading was adopted to grade xerostomia.[44] Patients were asked about his or her functional disability (ability to swallow food and interference with activities) and unstimulated whole mouth saliva was gathered by means of the pipette suction method. Prior to saliva collection, patients are asked not to eat, drink, or chew gum for at least 1 hour before collection. At the time of saliva collection, patients were asked to sit in an upright position, with eyes open, swallow, and then after swallowing, the patient bent their head forward and allowed saliva to collect in their mouth for 5 minutes. Saliva from the anterior floor of the mouth was collected by means of an appliance consisting of a micropipette holder (for use with 20-ml micropipettes) fitted with a 2 ml latex dropper bulb. The volume was recorded and flow rate (ml/min) was calculated.[45,46] The functional disability and flow rates were each scored from 1 to 3, respectively. A cumulative score (2-6) was calculated by adding the functional

disability and flow rate scores. Higher scores indicated greater functional disability and lower flow rates. A xerostomia grade ≥3 is considered clinically significant.[45]

Chemosensory Problems. Taste and smell perception was assessed by a questionnaire used to evaluate chemosensory function in AIDS and advanced cancer patients.[47,48] Patients rated their taste and smell function as "insignificant", "mild", "moderate", "severe", or "incapacitating". The tool yields a taste complaint score (0-10) and a smell complaint score (0-6). The total chemosensory complaint score (0-16) was calculated by summing the taste and smell complaint scores. Higher chemosensory complaint scores indicated worsening taste or smell impairment. A total chemosensory complaint score ≥7 is considered clinically significant.[48]

4.2.1 *Data Analyses*

Descriptive statistics were used to summarize subject characteristics. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Cancer location and stage were expressed as number and percentage, while age, weight, weight loss, BMI, energy intake, and QOL were expressed as mean and standard deviation. All variables were normally distributed. Repeated measures analysis of variance (ANOVA) was used to test the significance of energy intake, protein intake, weight, BMI, functional performance, QOL, and symptom changes over time. Correlations were investigated by Spearman's ρ. Independent t-test (2-tailed) were used to compare differences between treatment groups. Generalized estimating equations[49,50] (GEE) were used to estimate the impact of CRP and all evaluated symptoms association with energy intake, on weight loss, functional performance, and QOL. The GEE method accounts for the correlation due to repeated

observations available for each patient over time. We used GEE modeling approach to obtain robust parameter estimates and standard error with an exchangeable working correlation matrix, for a linear function. A standard model building technique was used to reach the most parsimonious model. In this method, variables which were significant at $p < 0.1$ at the univariate level were entered into a multivariate model. GEE was also used to estimate the impact of treatment (Chemotherapy Group vs No Chemotherapy) on energy intake, weight loss, functional performance, and QOL. A maximum α value of 0.05 was used for all statistical significance testing. Data analysis was performed using SPSS (version 16.0, SPSS, Chicago IL, 2006).

4.3 Results

Between March 2006 and July 2007, 38 patients completed this study. Characteristics of the patients are shown (Table 4.1). No tumour stage or age differences were detected in any variable. For the purposes of planned analysis patients were classified into two treatment groups. Patients receiving RT or surgery RT were classified in the no chemotherapy group. Patients receiving RTchemotherapy or surgery RTchemotherapy were classified in the chemotherapy group.

4.3.1 *Weight and Weight Loss*

Body weight, body mass index (BMI), and weight loss patterns for all patients, and the treatment groups during T1, T2, and T3 are summarized in Table 4.2. At T1, patients had a mean body weight of 84.2kg ±17.4 (range, 66.9- 102.5kg). More than 26 (68%) were overweight or obese (BMI >25) at study entry with a mean BMI of

28.1 ±4.8 kg/m^2 (range, 19.0-39.6), and 8 (21%) had a history of 5% weight loss in 6 months.

Overall, the body weights (kg) for all patients were significantly affected by time $F(2,44)=54.01$, $p\leq 0.0001$. There was a significant interaction between the treatment mode and body weight associated with it $F(2,44)= 11.7$, $p\leq 0.0001$. In general, all patients sustained a significant weight loss with 50% (19 of 38) of the patients losing >10% of their body weight (kg) from T1 to T2, and 34% (13 of 38) of the patients losing >5% of their body weight (kg) from T2 to T3. Body weight at T3 remained significantly lower than that at T1. Only 7% (3 of 38) of the patients had weight increases from T1 to T2, and 13% (5 of 38) had weight increases from T2 to T3. The probability of female patients having less weight loss over time than male patients was significant ($p< 0.008$).

4.3.2 *Energy Intake*

The mean energy intake and protein intake patterns during T1, T2, and T3, as well as comparisons between the no chemotherapy group and chemotherapy group are summarized in Table 4.3.

Overall, the energy intake (kcal/d) and protein intake (g/d) for all patients were significantly affected by time $F(2,68)=15.24$, $p\leq 0.0001$; $F(2,50.5)=14.3$ $p\leq 0.0001$, respectively. The interactions between the treatment mode and energy intake and protein intake were not significant $F(2,68)= 2.0$, $p=0.141$; $F(2,49)=14.3$ $p=0.321$, respectively. Energy intake and protein intake of all patients significantly decreased from T1 to T2. However, unlike the body weight pattern, energy intake and protein

intake significantly increased from T2 to T3. The energy intake and protein intake at T3 were not significantly different than those at T1.

The energy intakes of patients treated with chemotherapy and no chemotherapy are shown in Figure 4.2. Energy intake was not significantly different between the chemotherapy group versus the no chemotherapy group between T1, T2, and T3. At T1, the energy intake (kcal/d) for the majority of patients was derived from normal foods. At T2 however, the majority of patients derived approximately 60% energy intake from enteral supplements and/or other liquids. At T3, approximately 40% of the recorded energy intakes continued to be derived from enteral supplement and/or other liquids for most patients. For all patients, no correlation between energy intake (kcal/d) and weight loss (kg) were found at T1 ($r = .10$, $p=0.517$) or at T3 ($r = .16$, $p=0.351$). At T2 however, a positive correlation was found between energy intake and weight loss ($r = .37$, $p=0.02$).

4.3.3 *Functional Performance*

The functional performance patterns for all patients by treatment groups during T1, T2, and T3 are shown in Figure 4.3. The functional performance for all patients was significantly affected by time $F(2,64)=23.0$, $p\leq0.0001$. The majority of all patients at T1 perceived their functional performance as "normal with no limitation". However at T2, nearly 90% of all patients perceived reduced functional performance. While perceived functional performance improved at T3, over 50% of all patients continued to perceive a reduced functional performance. With regard to treatment type, patients treated with chemotherapy had poorer functional performance than those patients in the no chemotherapy group. In the no chemotherapy group, functional performance

declined from T1 to T2, but the change was not significant. At T3, the groups' functional performance scores improved and were better than the functional performances at T1. In the chemotherapy group however, the decline from T1 to T2 was significant, and thereafter function performance improved between T2 and T3 but not to T1 levels of performance. Independent t-test showed that on average during T2 and T3, patients in the chemotherapy group had poorer functional performance (1.4±0.7, $p<0.001$; 0.95±0.57, $p<0.0001$, respectively), than patients in the no chemotherapy group (0.84±0.37; 0.16±0.38).

For all patients, significant relationships between functional performance and weight loss (kg) were found at T1 ($r = .40$, $p<0.01$), T2 ($r = .42$, $p<0.008$), and T3 ($r = .41$, $p<0.015$). There was a non-significant relationship between functional performance and energy intake (kcal/d) at T1 ($r = -.28$, $p= 0.084$), and at T2, no correlation was found between functional performance and energy intake ($r = -.21$, $p= 0.20$). However, a significant negative relationship between functional performance and energy intake was found at T3 ($r = -.47$, $p<0.006$).

4.3.4 *Quality of Life*

The mean cumulative and domain QOL scores patterns for all patients by treatment group and T1, T2, and T3 data collection during the treatment periods are summarized in Table 4.4. The QOL for all patients was significantly affected by time $F(2,64)=78.0$, $p\leq0.0001$. Overall, the QOL cumulative and domain scores were high at T1, thereafter scores significantly decreased during T2. At T3, most QOL scores improved.

Independent t-test showed that on average during T2, patients in the chemotherapy group had significantly poorer cumulative QOL scores (536±131, $p<0.003$), than patients in the no chemotherapy group (667±101)

For all patients, no relationship between mean cumulative QOL and weight loss (kg) was found at T1 or T3 ($r = .25$; $r = .28$, $p>0.05$, respectively). But at T2, a negative relationship between mean cumulative QOL and weight loss (kg) was found ($r = -.42$, $p<0.0001$). There was a no relationship between mean cumulative QOL and energy intake (kcal/d) at T1 ($r = .17$, $p=0.28$), but during T2 and T3, a positive relationship was found between mean cumulative QOL scores and energy intake ($r = .39$, $p<0.01$; $r = .32$, $p<0.07$, respectively).

4.3.5 *Systemic Inflammation – CRP*

Mean CRP serum concentration patterns for all patients by treatment groups during T1, T2, and T3 are shown in Figure 4.4. The CRP serum concentration for all patients was significantly affected by time $F(2, 52.0) = 9.2$, $p\leq0.001$. Evidence of systemic inflammation (CRP $\geq$ 10mg/l) was found in 10% (4 of 38) of all patients at T1. But at T2, evidence of systemic inflammation rose to 39% (15 of 38), and during T3 declined again to 15% (6 of 38) of all patients.

An equal number of patients in both treatment groups showed evidence of systemic inflammation at T1. However at T2, 53% (13 of 25) of the chemotherapy group had systemic inflammation presence compared to 15% (2 of 13) of the no chemotherapy group ($p<0.032$). At T3, evidence of systemic inflammation declined to 16% (4 of 25) in the chemotherapy group, and in the no chemotherapy group evidence of systemic inflammation remained at 15%.

Interestingly, no relationship between CRP serum concentrations and energy intake, weight loss, functional performance, and quality of life was found at T1, T2, or T3.

4.3.6 *Nutrition Impact Symptoms*

The clinical significance of a symptom was determined by the clinical relevant acuity of symptom score. Table 4.5 shows clinically significant symptoms for all patients in each treatment group during T1, T2, and T3. Dysphagia, pain, loss of appetite, and xerostomia were the most common symptoms found in patients at T1. For all patients, the frequency of symptoms nearly quadrupled at T2 compared to T1. Although the occurrence of symptoms diminished, nearly 50% of all patients still had symptom presence at T3.

The symptom scores for all treatment groups during the data collection points are summarized in Table 4.6. Interestingly, no significant differences between the treatment groups were found at T1, T2, or T3.

4.3.7 *Treatment, Systemic Inflammation and Nutrition Impact Symptoms Predictors of Energy Intake, Weight Loss, Functional Performance, and QOL*

The results of the GEE univariate and multivariate models of predictors of energy intake, weight loss, functional performance and QOL between treatment groups over time are summarized in Tables 4.7a and 4.7b. The top portion of GEE univariate models (Table 4.7a), shows that treatment was only a predictor of weight loss. However, our other comparisons show that there are clear differences in the systemic inflammation and symptoms within each treatment group. Therefore, we decided to apply the GEE modeling to each treatment group separately. In the GEE multivariate models (Table 4.7b) for the no chemotherapy group, systemic inflammation was not a

predictor of any outcome, whereas in the chemotherapy group, systemic inflammation was a significant predictor of weight loss and reduced functional performance. The symptom predictors were also different between the treatment groups. When the groups were combined we found that timed swallowing capacity was a significant predictor of energy intake, weight loss, functional performance, and QOL. But, timed swallowing capacity was only a significant predictor of energy intake in the chemotherapy group. Also notably, loss of appetite, pain and xerostomia grade were significant predictors of weight loss in the chemotherapy group, but were not in the no chemotherapy group.

4.4 Discussion

These results support the hypothesis that symptoms and systemic inflammation associated with the addition of chemotherapy to other forms of treatment for HNC results in significant declines in dietary intake, weight loss, functional performance, and quality of life over time. Interestingly, these results were not evident when treatment groups were investigated together. We are currently engaging in ongoing study to explore these findings in more detail.

4.4.1 *Weight loss and energy intake*

In the past, the majority of HNC patients were described as cachetic, but we found that the body weight and BMI of most patients at presentation resembled the overweight and obese prevalence in the general Canadian population. While body weight and BMIsat study entry might suggest that HNC patients are well nourished these indicators must be framed within the context of future losses. We found that all patients lost body weight over time. Notable were the weight losses sustained by

patients receiving adjuvant chemotherapy, who had body weight losses upwards of 23% within a 20 week period, compared to the 13% body weight loss of patients not receiving chemotherapy over that same time period. We also found that significant weight losses occurred during treatment and continued to progress after treatment. Similar patterns of losses in body weight in HNC patients have been reported in other studies.[24,51] This pattern of weight loss is comparable with that seen in severe injury models – like burns or trauma. The severe burn injury model is characterized by a rapid loss in body weight with preservation of body fat and severe losses in lean tissue mass. Silver et al.(2007) reported that lean body mass accounted for 71% of the body mass loss in HNC patients undergoing RT chemotherapy. [24] The depletion of lean body mass can have profound consequences on wound healing, functional performance, and QOL. Thus, these results suggest that the high body weight and BMI at presentation may not protect patients from rapid protein catabolism and malnutrition over the course of treatment. Additionally, these results suggest that there is a need for early nutritional support of HNC patients, particularly for those patients undergoing adjuvant chemotherapy protocols and that nutritional support is likely required a over the course of treatment. Interestingly, female patients were less inclined to lose weight than male patients. Similar gender differences in HNC patients have been reported by others.[8]

Energy intakes declined during treatment but thereafter increased. However, despite these increases patients continued to lose weight. Although counterintuitive, the dissonance between energy intake and weight loss may be explained in terms of a negative energy balance. We calculated that the cumulative energy deficits of patients

not receiving chemotherapy could be in the order of 30,313 kcal in a 20 week period, while patients receiving adjuvant chemotherapy may have had cumulative energy deficits upwards of 122,640 kcal over the same time period. Thus, it follows that with cumulative deficits in energy intake resulted in weight loss at T3. Computation modeling work of weight loss patterns showed that despite increases in energy intakes during a re-feeding period, weight losses continued in the cachexic cancer patient.[52] Thus, using the computation modeling work to project weight patterns in this cohort of patients, we suspect that with the patient's average energy intake at T3 (re-feeding intakes) it is likely that weight loss will continue, as patients are still in a state of negative energy balance. This data provides further evidence for the need to provide nutritional support and interventions during and following treatment time for all HNC patients, particularly those patients receiving adjuvant chemotherapy

Most patients' T1 and T3 energy intakes (30.1kcal/kg/d to 31.0 kcal/kg/d, respectively) were comparable to the ESPEN's recommended estimated daily energy requirements between 30 – 35 kcal/kg/d for cancer patients.[38] Yet, we found that nearly 50% of the patients at T1 and 71% of the patients at T3 taking in the recommended number of calories lost weight. This finding suggests that recommended energy requirements may be underestimating the patient's metabolic demands. Garcia-Peris et al. (2005) compared the resting energy expenditure by indirect calorimetry with the value estimated by the Harris-Benedict formula and found that the Harris-Benedict formula underestimated the patients' resting energy expenditure.[51] Goncalves Dias, Marucci, Nadalin and Waitzberg (2005) counseled HNC patients undergoing RT to consume 40kcal/kg/d and found that patients who did

so were able to maintain their body weights.[53] Further research evaluating resting energy expenditure during various treatments may help to establish adequate energy intake requirements for HNC patients.

4.4.2 *Functional performance*

We found that nearly 90% of all patients at T2 described their functional performance as reduced and 50% continued to describe their functional performance as reduced at T3. Reduced functional performance has been reported to be associated with systemic inflammation, weight loss, particularly loss of lean tissue, and survival.[54-57] While we did find correlations between functional performance and weight loss, only a weak correlation was found between functional performance and elevated CRP serum concentrations in the GEE modeling. It is noteworthy, that all nutrition impact symptoms at the univariate level were significantly associated with functional performance in the GEE modeling. These findings support the importance of ongoing attention to symptom management. We also found that patients treated with adjuvant chemotherapy had significantly poorer functional performance than patients not receiving adjuvant chemotherapy. This difference in functional performance may be due to the significant differences in weight loss and systemic inflammation between the treatment groups.

4.4.3 *Quality of Life*

Our scores patterns from the UWQOL are consistent with those of prior studies which showed similar QOL score patterns.[58,59] It is noteworthy that cumulative and domain scores including activity, recreation and swallowing were significantly lower in patients receiving chemotherapy. The reasons for the declines in activity and

recreation between the treatment groups at T2 may be related to differences in weight loss and the additional use of anti-nausea medications like ondansetron, which is known to cause drowsiness. The reasons for the decline in the swallowing domain may be related to effects of the chemotherapy drugs on the irradiated areas. Additionally, we found that the declining QOL scores during T2 were associated with weight loss. Previously, a similar association between QOL and weight loss was reported in HNC patients.[60] While associations between QOL and serum CRP concentrations in other tumour groups were previously identified,[54,56] we found that serum CRP concentrations were only significant associated with QOL at the univariate level of GEE modeling. Not surprising were the significant associations between QOL and all nutrition impact symptoms at the univariate level of GEE modeling. Previously, similar associations between QOL and nutrition impact symptoms were reported in HNC patients.[61]

4.4.4 *Systemic Inflammation*

As expected serum CRP concentrations increased during T2. Ellegard and Bosaeus [62] have suggested that increased CRP may be related to primary stress of treatment and reduced energy intake, but we did not find a correlation between serum CRP concentrations and energy intake at T2 or overall energy intake. We did find that that serum CRP concentrations were significantly associated with weight loss at the univariate level of GEE modeling. Additionally, serum CRP concentrations were significant predictors of weight loss and functional performance for patients in the chemotherapy group.

4.4.5 *Nutrition Impact Symptoms*

Although symptoms acuity increases during treatment and many are known to be present a year after treatment, little was known about their impact on dietary intake and weight loss. The impetus to seek out and take in energy can be undermined in the presence of symptoms. For example, patients whose swallowing capacities ≤ 5ml/min were only able to consume on average 17.3 kcal/kg/d or 1265 kcal/d. Similarly, patients with pain complaints ≥ 3 were taking on average 22.0 kcal/kg/d or 1607 kcal/d. Although many others have reported relationships between some of the variables in this study, they generally relied on self-report measures. Our results are based primarily on both self-report and objective measures and evaluated the combined effect of energy intake, weight loss, functional performance, and QOL. GEE modeling demonstrated that all nutrition impact symptoms were associated with dietary intake and weight loss at the univariate level. However, only pain and timed swallowing capacity were associated with energy intake and weight loss at the multivariate level. Interestingly, we found that symptom behaviors differed between the treatment groups. For example, loss of appetite was a significant predictor of energy intake in the no chemotherapy but not in the chemotherapy group. The difference may be related to the use of dexamethasone in the chemotherapy group. On the other hand, pain was a significant predictor of energy intake in the chemotherapy group but not in the no chemotherapy group. The difference may be related to the additional compromises related to treatment. However, regardless of treatment, symptoms influences on energy intake and weight loss are important among head and neck cancer patients.

4.5 Conclusion

The findings of this present study suggest that the current approach of nutrition support care may not be effectively meeting the needs of patients. Given that patients receiving adjuvant chemotherapy sustain significant weight losses it may be necessary to plan earlier nutrition intervention. Further, the realization that patients continue to lose weight while consuming 30kcal/kg/d also suggests that re-evaluation of recommended energy requirements for HNC patients may be required. The understanding that symptoms contribute to the decline of energy intake, weight loss, functional performance, and QOL over time may help in the development of appropriate symptom management, including nutrition support to prevent weight loss in HNC patients.

Table 4.1 Patient characteristics at Baseline (T1)

Characteristic	*Number of patients (%) (n=38)*
Age, y	
Mean ± SD	54 ± 11
Median, Range	54 (24-79)
Age ≥65	6 (15.7)
Sex	
Male	31 (81.5)
Female	7 (18.4)
Tumour stage	
T0	2 (5.1)
T1	7 (18.4)
T2	12 (31.5)
T3	10 (26.3)
T4	6 (15.7)
Not staged	1 (2.6)
Tumour site	
Lip/oral cavity	5 (13.1)
Pharynx	21 (55.2)
Larynx	8 (21.0)
Salivary Gland	2 (5.2)
Primary site unknown	2 (5.2)
Mode of treatment	
Radiation therapy (RT)	6 (15.7)
Surgery RT	7 (18.4)
RT chemotherapy	11 (28.9)
Surgery RTchemotherapy	14 (36.8)
Overall Treatment Mode	
No Chemotherapy	13 (34.2)
Chemotherapy	25 (65.7)

Table 4.2 Body weight, body mass index (BMI), and weight loss patterns of Head and Neck Cancer Patients and treatment groups during treatment periods of T1, T2, and T3

Weight	Baseline (T1)	Treatment (T2)	Follow-up (T3)	
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Mean number of days from baseline		70 days	140 days	
All Patients (n=38)				
Body Weight (kg)	84.2±17.4$^{\dagger\ddagger\Pi}$	76.1±16.8$^{*\ddagger\Pi}$	73.6±15.0$^{*\dagger\Pi}$	
Body Mass Index (kg/m^2)	28.1±4.9†‡	25.4±5.1*‡	24.6±4.8*†	
Weight loss (kg)	0.2±3.8†‡	-8.5±6.2*‡	-2.3±3.4*†	
Percent weight loss between treatment periods	0.5±4.4†‡	-9.4±7.8 *‡	-2.8±4.6*†	
Percent weight loss between baseline and follow-up				-11.6±8.9
No Chemotherapy (n=13)				
Body Weight (kg)	83.3±19.0†‡	79.8±16.2*	78.1±16.0*	
Body Mass Index (kg/m^2)	28.7±5.8†‡	27.5±4.9*§	26.9±5.1*§	
Weight loss (kg)	-0.7±4.7	-3.5±4.8§	-1.2±3.6	
Percent weight loss between treatment periods	-0.6±5.1	-3.5±5.9§	-1.9±3.5	
Percent weight loss between baseline and follow-up				-5.7±7.5§
Chemotherapy (n=25)				
Body Weight (kg)	85.4±17.6†‡	74.0±17.0*‡	71.1±14.7*†	
Body Mass Index (kg/m^2)	27.8±4.5†‡	24.2±4.9$^{*\ddagger\Pi}$	23.2±4.2$^{*\dagger\Pi}$	
Weight loss (kg)	1.0±3.2†‡	-11.4±5.2$^{*\ddagger\Pi}$	-3.6±2.3*†	
Percent weight loss between treatment periods	1.2±3.9†‡	-13.4±6.4$^{*\ddagger\Pi}$	-3.9±3.5*†	
Percent weight loss between baseline and follow-up				-15.3±7.7

* $p<0.05$ vs Baseline by analysis of variance (ANOVA) repeated measures

† $p<0.05$ vs Treatment by ANOVA repeated measures

‡ $p<0.05$ vs Follow-up by ANOVA repeated measures

§ $p<0.05$ Independent t-test between No Chemotherapy vs Chemotherapy vs Chemotherapy

Π $p<0.05$ Interaction by analysis of variance (ANOVA) repeated measures

Table 4.3 Energy intake patterns of Head and Neck Cancer Patients and treatment groups during treatment period of T1, T2, and T3

Energy Intake	Baseline (T1)	Treatment (T2)	Follow-up (T3)
	Mean ± SD	Mean ± SD	Mean ± SD
All Patients (n=38)			
Energy intake (kcal/d)	2501±618[†]	1552±1009[*‡]	2202±676[†]
Energy intake(kcal/kg/d)	31.0±1.5[†]	20.3±2.4[*‡]	30.1±1.7[†]
Protein Intake (g/d)	108±34[†]	63±39[*†]	108±57[†]
Percent of patients losing weight at this energy intake	47%	97%	71%
No Chemotherapy (n=13)			
Energy intake (kcal/d)	2388±481	1905±929	2438±736
Energy intake(kcal/kg/d)	30.2±10.0	24.9±13.4	31.8±8.5
Protein Intake (g/d)	108±29[*]	78±40[*]	106±48
Percent of patients losing weight at this energy intake	61%	76%	61%
Chemotherapy (n=25)			
Energy intake (kcal/d)	2565±687[*‡]	1351±1018[*‡]	2064±612[*†]
Energy intake(kcal/kg/d)	31.5±8.1[†]	18.3±14.2[*‡]	29.0±10.4[†]
Protein Intake (g/d)	108±38[†]	54±37[*‡]	106±68[†]
Percent of patients losing weight at this energy intake	44%	100%	72%

[*] $p<0.05$ vs Baseline by analysis of variance (ANOVA) repeated measures

[†] $p<0.05$ vs Treatment by ANOVA repeated measures

[‡] $p<0.05$ vs Follow-up by ANOVA repeated measures

Table 4.4 University of Washington Quality of Life score patterns of Head and Neck Cancer Patients and treatment groups during treatment periods of T1, T2, and T3

UWQOL Scores	Baseline (T1)	Treatment (T2)	Follow-up (T3)
All Patients (n=38)	mean ±SD	mean ±SD	mean ±SD
Cumulative (1-1000)	890±100*†	600±125*‡	690±155*†
Domain (1-100)			
Pain	81±22†	55±25*‡	77±21†
Appearance	89±16*†	67±20*	69±23*
Activity	82±21*†	53±23*‡	65±20*†
Recreation	86±20*†	53±26*‡	71±20*†
Swallowing	86±20*†	42±23*‡	65±24*†
Chewing	90±23†	61±39*	85±15†
Speech	92±15†	76±29*	86±16†
Shoulder	92±14†	73±36*	71±36*
Taste	84±26*†	25±35*‡	50±33*†
Saliva	95±9†	56±34*	50±33*
No Chemotherapy (n=13)			
Cumulative (1-1000)	882±110†	667±101*§	750±158*
Domain (1-100)			
Pain	84±24†	53±17*	81±18†
Appearance	92±12*†	75±16*	75±23*
Activity	86±19†	67±15*§	70±17*
Recreation	86±19†	71±22*§	77±19*
Swallowing	82±23†	57±21*§	77±24*†§
Chewing	94±10†	71±35*	91±12†
Speech	92±12	81±27	85±12
Shoulder	92±12	78±32	75±36
Taste	76±27†	34±40*‡	62±36†
Saliva	94±10†	67±25*	58±35*
Chemotherapy (n=25)			
Cumulative (1-1000)	881±137*†	536±131*‡	658±110*†
Domain (1-100)			
Pain	80±20†	56±27*‡	75±23†
Appearance	88±17†	64±21*	69±23*
Activity	80±20*†	47±24*‡	61±21*†
Recreation	87±21*†	45±23*‡	69±20*†
Swallowing	88±25*†	34±20*‡	59±21*†
Chewing	89±28†	57±41*	82±16*
Speech	92±17†	74±30*	86±18†
Shoulder	92±15†	70±38*	70±36*
Taste	88±25*†	20±32*‡	41±29*†
Saliva	96±20†	51±37*	45±32*

* $p<0.05$ vs Baseline by analysis of variance (ANOVA) repeated measures

† $p<0.05$ vs Treatment by ANOVA repeated measures

‡ $p<0.05$ vs Follow-up by ANOVA repeated measures

§ $p<0.05$ Independent t-test between No Chemotherapy vs Chemotherapy

Table 4.5 Frequency of clinically significant nutrition impact symptom in Head and Neck Cancer Patients and treatment groups during treatment periods of T1, T2, and T3

Nutrition Impact Symptom	Baseline (T1) (%)	Treatment (T2) (%)	Follow-up (T3) (%)
All patients (n=38)			
Loss of Appetite	7 (18)	26 (68)	12 (31)
Pain	8 (21)	28 (73)	11 (29)
Dysphagia	10 (26)	29 (76)	18 (47)
Mucositis	0 (0)	11(29)	0 (0)
Xerostomia	7 (18)	28 (73)	25 (66)
Chemosensory Complaints	3 (8)	32 (84)	17 (44)
No Chemotherapy (n=13)			
Loss of Appetite	1 (8)	6 (46)	4 (31)
Pain	3 (23)	7 (53)	3 (23)
Dysphagia	5 (38)	8 (62)	5 (39)
Mucositis	0 (0)	4 (31)	0 (0)
Xerostomia	3 (23)	11 (85)	8 (61)
Chemosensory Complaints	1 (8)	11 (85)	4 (31)
Chemotherapy (n=25)			
Loss of Appetite	6 (24)	20 (80)	8 (32)
Pain	5 (20)	21 (84)	9 (36)
Dysphagia	5 (20)	21 (84)	13 (52)
Mucositis	0 (0)	7 (28)	0 (0)
Xerostomia	4 (16)	17 (68)	17 (68)
Chemosensory Complaints	2 (8)	21 (84)	13 (52)

Table 4.6 Symptom patterns of Head and Neck Cancer Patients and treatment groups during treatment period of T1, T2, and T3

Nutrition Impact Symptoms	Baseline (T1)	Treatment (T2)	Follow-up (T3)
	Mean ± SD	Mean ± SD	Mean ± SD
All Patients (n=38)			
Loss of Appetite (0-5)	1.4±0.9†‡	3.2±1.4*‡	2.2±1.4*†
Pain (0-5)	1.5±1.1†	3.5±1.5*	2.0±1.1†
Swallowing Capacity (ml/min)	12.9±4.7†	6.6±4.9*‡	11.0±5.0†
Oral Mucositis Grade (0-9)	0.1±0.4†‡	3.0±2.3*‡	0.7±1.1*†
Xerostomia Grade (2-6)	3.3±1.3†	5.1±1.0*	4.7±1.2*
Chemosensory Complaints (0-16)	1.5±2.7†‡	9.1±2.9*‡	6.6±2.6*†
No Chemotherapy (n=13)			
Loss of Appetite (0-5)	1.5±1.1†	3.0±1.3*	2.1±1.4
Pain (0-5)	1.9±1.5	3.0±1.4‡	1.5±0.7†
Swallowing Capacity (ml/min)	11.5±6.0	8.5±4.3	11.0±4.6
Oral Mucositis Grade (0-9)	0.1±0.5†	2.0±2.2*‡	0.4±0.6†
Xerostomia Grade (2-6)	3.3±1.5†	5.2±.59*	4.4±1.3*
Chemosensory Complaints (0-16)	1.7±2.5†‡	8.0±2.7*‡	5.8±3.8*†
Chemotherapy (n=25)			
Loss of Appetite (0-5)	1.5±1.0†‡	3.5±1.8*‡	2.2±1.4*†
Pain (0-5)	1.5±1.0†‡	3.8±1.5*‡	2.3±1.2*‡
Swallowing Capacity (ml/min)	13.0±4.7†	5.6±4.9*‡	11.0±4.7†
Oral Mucositis Grade (0-9)	0.1±0.3†‡	3.5±2.2*‡	0.9±1.3*†
Xerostomia Grade (2-6)	3.3±1.2†	5.0±1.2*	4.4±1.3*
Chemosensory Complaints (0-16)	1.9±3.8†‡	9.7±2.8*‡	7.2±2.1*†

* $p<0.05$ vs Baseline by analysis of variance (ANOVA) repeated measures

† $p<0.05$ vs Treatment by ANOVA repeated measures

‡ $p< 0.05$ vs Follow-up by ANOVA repeated measures

§ $p<0.05$ Independent t-test between No Chemotherapy vs Chemotherapy vs Chemotherapy

¦ $p< 0.05$ Interaction by ANOVA repeated measures

Table 4.7a Generalized Estimating Equations Univariate Model of Predictors of Energy Intake, Weight loss, Functional Performance, and Quality of Life of Head and Neck Cancer Patients and treatment groups during the treatment periods of T1, T2, and T3

Variable	Energy Intake (kcal/d)				Weight loss (kg)				Functional Performance (0-3)				UW-QOL (0-1000)			
	β	S.E.	p-value	95% CI	β	S.E.	p-value	95% CI	β	S.E.	p-value	95% CI	β	S.E.	p-value	95% CI
Treatment																
Chemotherapy/No chemo group	-177.14	141	0.212	-524.3 - 170.0	-2.48	0.79	0.002	-7.34 - 2.38	-0.18	0.15	0.222	-0.18 - 0.55	-49.33	41.6	0.237	-146.0 - 47.3
Systemic Inflammation																
C-reactive protein (mg/l)	-2.8	1.5	0.068	-8.2 - 2.7	-0.030	0.0	0.000	-0.08 - 0.02	0.00	0.00	0.007	-0.0 - 0.0	-0.63	0.24	0.008	-1.8 - 0.6
Nutrition Impact Symptoms																
Loss of Appetite (0-5)	-242.8	48.3	0.000	-718.6 - 233.0	-1.600	0.4	0.000	-4.7 - 1.5	0.27	0.04	0.000	-0.26 - 0.79	-72	9.3	0.000	-213.1 - 69.1
Pain (0-5)	-285.5	46.5	0.000	-845.0 - 274.0	-2.300	0.3	0.000	-6.8 - 2.2	0.23	0.04	0.000	-0.22 - 0.68	-80.6	7.2	0.000	-238 5 - 77.3
Swallowing Capacity (ml/min)	66.7	14.1	0.000	-64.0 - 197.4	0.400	0.1	0.001	-0.4 - 1.2	-0.07	0.01	0.000	-0.20 - 0.06	17	4.2	0.000	-16.3 - 50.3
Oral Mucositis Grade (0-9)	-172.6	40.5	0.000	-510.8 - 165.6	-1.500	0.2	0.000	-4.4 -1.4	0.13	0.02	0.000	-0.12 - 0.37	-47.7	5.6	0.000	-141.1 - 45.7
Xerostomia Grade (2-6)	-160.2	61.1	0.009	-474.1 - 153.7	-1.000	0.3	0.002	-3.0 - 1.0	0.20	0.04	0.000	-0.19 - 0.59	-68.6	10.2	0.000	-203.0 - 65.8
Chemosensory problems (0-16)	-77.2	15.6	0.000	-228.5 - 74.1	-0.600	0.1	0.000	-1.8 - 0.6	0.08	0.02	0.000	0.08 - 0.25	-30.5	2.9	0.000	-90.2 - 29.0
No Chemotherapy (n=13)																
Systemic Inflammation																
C-reactive protein (mg/l)	5.5	15.7	0.725	-5.28 - 16.28	-0.03	0.06	0.599	-0.08 - 0.02	0.001	0.004	0.795	-0.0 - 0.0	-1.4	1.4	0.325	-4.1 - 1.3
Nutrition Impact Symptoms																
Loss of Appetite (0-5)	-219.4	68.6	0.001	-649.4 - 210.6	-0.878	0.46	0.06	-2.5 - 0.84	0.12	0.03	0.002	-0.11 - 0.35	-57.7	11.8	0.000	-170.7 - 55.39
Pain (0-5)	-171.9	100.6	0.088	-508.8 - 165.0	-1.2	0.39	0.002	-3.5 - 1.1	0.12	0.05	0.022	-0.11 - 0.35	-57.9	14.1	0.000	-171.3 - 55.5
Swallowing Capacity (ml/min)	42.8	16.6	0.010	-41.0 - 126.6	0.23	0.157	0.155	-.22 - 0.6	-0.022	0.008	0.012	-0.65 - 0.02	12.7	3.4	0.000	-12.1 - 37.5
Oral Mucositis Grade (0-9)	-101.6	71.2	0.154	-300.7 -97.5	-1.00	0.28	0.000	-2.96 - 0.96	0.06	0.03	0.099	-0.05 - 0.17	-38.7	5.6	0.000	-114.5 - 37.1
Xerostomia Grade (2-6)	-28.4	88.78	0.749	-84.0 -27.2	-0.05	0.45	0.897	-0.14 - 0.04	0.13	0.05	0.007	-0.12 - 0.38	-56.3	15.4	0.000	-166.6 - 54.0
Chemosensory problems (0-16)	-41.3	25	0.098	-122.2 -39.6	-0.248	0.17	0.164	-0.73 - .23	0.05	0.02	0.012	-0.04 - 0.14	-26.9	4.6	0.000	-79.6 - 25.8
Chemotherapy (n=25)																
Systemic Inflammation																
C-reactive protein (mg/l)	-13.3	5.7	0.020	-39.3 -12.7	-0.15	0.04	0.000	-0.44 - 0.14	0.021	0.005	0.000	-0.02 - 0.06	-3.7	0.75	0.000	-10.9 - 3.5
Nutrition Impact Symptoms																
Loss of Appetite (0-5)	-246.1	65.3	0.000	-728.4 - 236.2	-1.68	0.55	0.002	-4.97 -1.61	0.324	0.04	0.000	-0.31 - 0.95	-75.2	12.14	0.000	-222.5 - 72.1
Pain (0-5)	-328.2	47.7	0.000	-971.4 -315.0	-2.76	0.38	0.000	-8.16 - 2.64	0.241	0.05	0.000	-0.23 - 0.71	-84.04	7.6	0.000	-248.7 - 80.6
Swallowing Capacity (ml/min)	72.8	18.4	0.000	-69.8 - 215.4	0.399	0.16	0.016	-0.38 - 1.18	-0.078	0.01	0.000	-0.23 - 0.07	18.33	5.7	0.001	-17.5 - 54.2
Oral Mucositis Grade (0-9)	-194.6	51.6	0.000	-576.0 - 186.8	-1.5	0.27	0.000	-4.4 - 1.4	0.131	0.03	0.000	-0.12 - 0.38	-47.6	7.3	0.000	-140.8 - 45.6
Xerostomia Grade (2-6)	-225.8	79.1	0.004	-668.3 -216.7	-1.15	0.42	0.007	-3.4 - 1.1	0.245	0.04	0.000	-0.23 - 0.72	-71.8	12.1	0.000	-212.5 - 68.9
Chemosensory problems (0-16)	-87.4	19.2	0.000	-258.7 - 83.9	-0.679	0.2	0.001	-2.0 -0.65	0.11	0.017	0.000	-0.1 - 0.32	-31.2	3.5	0.000	-92.3 - 29.9

Table 4.7b Generalized Estimating Equations Multivariate Model of Predictors of Energy Intake, Weight loss, Functional Performance, and Quality of Life of Head and Neck Cancer Patients and treatment groups during the treatment period of T1, T2, T3

Variable	Energy Intake (kcal/d)				Weight loss (kg)				Functional Performance (0-3)				UW-QOL (0-1000)			
	β	S.E.	p-value	95% CI	β	S.E.	p-value	95% CI	β	S.E.	p-value	95% CI	β	S.E.	p-value	95% CI
Systemic Inflammation																
C-reactive protein (mg/l)					-0.01	0.0	0.124	-2.1 - 0.7								
Nutrition Impact Symptoms																
Loss of Appetite (0-5)	-102.7	55.9	0.066	-303.9 - 98.5					0.19	0.03	0.000	-0.19 -0.57				
Pain (0-5)	-174.1	56.9	0.002	-515.3 - 167.1	-1.12	0.3	0.000	-3.1 - 1.0					-44.8	7.1	0.000	-132.6 - 43.0
Swallowing Capacity (ml/min)	38.6	12.9	0.003	-37.0 -114.2	0.18	0.1	0.043	-0.2 - 0.5	-0.04	0.01	0.001	-0.12 - 0.04	5.4	2.4	0.026	-5.1 - 15.9
Oral Mucositis Grade (0-9)					-1.00	0.3	0.001	-3.0 - 1.0								
Xerostomia Grade (2-6)									0.09	0.04	0.039	-0.09 - 0.27	-18.5	7.5	0.015	-54.7 - 17.7
Chemosensory problems (0-16)													-17.1	2.8	0.000	-50.6 - 16.4
No Chemotherapy (n=13)																
Nutrition Impact Symptoms																
Loss of Appetite (0-5)	-201.30	66.80	0.003	-595.8 - 193.2					0.098	0.030	0.006	-0.09 - 0.2				
Pain (0-5)					-0.670	0.430	0.019	-1.9 - 0.6					-31.1	11.70	0.008	-92.0 - 29.8
Swallowing Capacity (ml/min)	32.06	14.16	0.024	-30.7 - 94.8					-0.018	0.008	0.029	-0.05 - 0.01	6.40	2.30	0.005	-6.1 - 18.9
Oral Mucositis Grade (0-9)					-0.700	0.290	0.011	-2.0 - 0.6								
Xerostomia Grade (2-6)									0.084	0.040	0.052	-0.08 - 0.24				
Chemosensory problems (0-16)													-21.90	2.60	0.000	-64.8 - 21.0
Chemotherapy (n=25)																
Systemic Inflammation																
C-reactive protein (mg/l)					-0.127	0.030	0.027	-0.3 - 0.12	0.016	0.005	0.003	-0.01 - 0.04				
Nutrition Impact Symptoms																
Loss of Appetite (0-5)					-1.000	0.430	0.024	-2.96 - 0.96	0.274	0.044	0.000	-0.26 - 0.81				
Pain (0-5)	-199.40	54.30	0.000	-590.2 - 191.4	-1.070	0.380	0.015	-3.16 - 1.02					-57.50	8.10	0.000	-170.2 - 55.2
Swallowing Capacity (ml/min)	41.60	15.56	0.007	-39.9 - 123.1	0.112	0.080	0.169	-0.10 - 0.33								
Oral Mucositis Grade (0-9)	-75.40	42.00	0.073	-223.1 - 72.3	-0.760	0.370	0.040	-2.24 - 0.72								
Xerostomia Grade (2-6)					-1.060	0.400	0.015	-3.13 - 1.0	0.187	.0.043	0.000	-0.17 - 0.55	-25.00	9.30	0.008	-74.0 - 24.0
Chemosensory problems (0-16)													-16.70	4.20	0.000	-49.4 -16.0

Baseline (T1) Mean Days (SD)	Treatment (T2) Mean Days from Baseline (SD)	Follow-up (T3) Mean Days from Baseline (SD)
RT 0 (0)	56 (± 8)	124 (± 10)
Surgery RT 0 (0)	84 (± 10)	154 (± 12)
RTchemotherapy 0 (0)	64 (± 6)	120 (± 12)
Surgery RTchemotherapy 0 (0)	98 (± 10)	164 (± 8)
No Chemotherapy	70 (± 10)	140 (± 10)
Chemotherapy	81 (± 12)	144 (± 12)

Figure 4.1 Mean Days to Assessment for each treatment group and treatment mode.

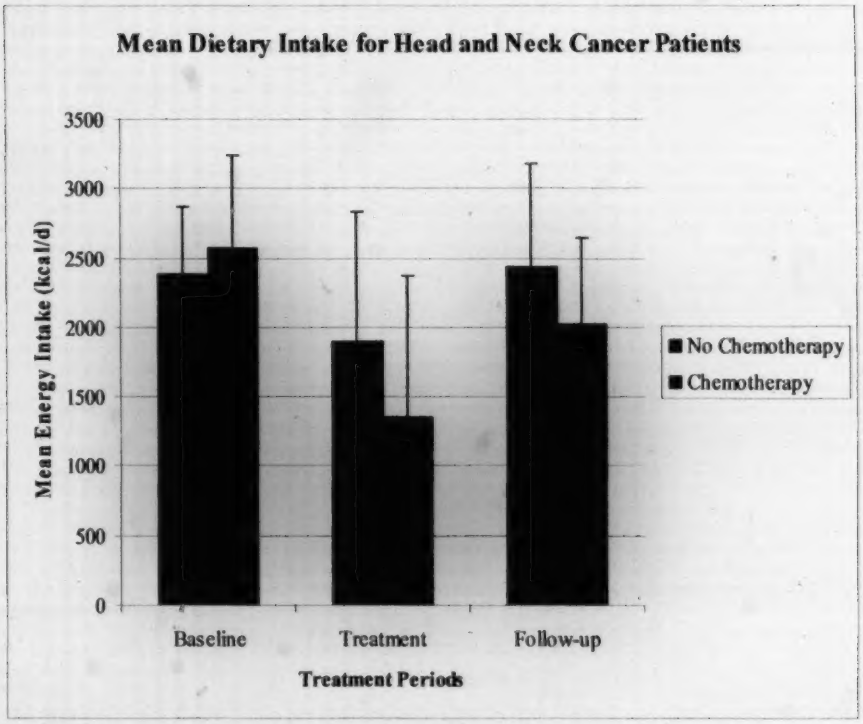

Figure 4.2 Mean dietary intake patterns during treatment periods for: No Chemotherapy Group vs Chemotherapy Group.
No Chemotherapy Group - energy intake deficit from Baseline to Treatment = -33,810 kcal energy intake; from Treatment to Follow-up = +3,500 kcal; Total energy deficit from Baseline to Follow-up = -30,313 kcal. Chemotherapy Group - energy intake deficit from Baseline to Treatment = -84,980 kcal; from Treatment to Follow-up = -37,660 kcal; Total energy deficit from Baseline to Follow-up = -122,640 kcal.
The total energy deficit for patients in the No Chemotherapy Group was based on: = [(mean energy intake (T2) - mean energy intake (T1) * 70 days] + [(mean energy intake (T3) - mean energy intake (T1)) * 70 days].
Total energy deficit = [(1,905kcal/d - 2,388 kcal/d) * 70 days] + [(3,500kcal/d - 2,388 kcal/d) * 70 days] or [(483) * 70] +[(50) * 70] = -33,810 kcal

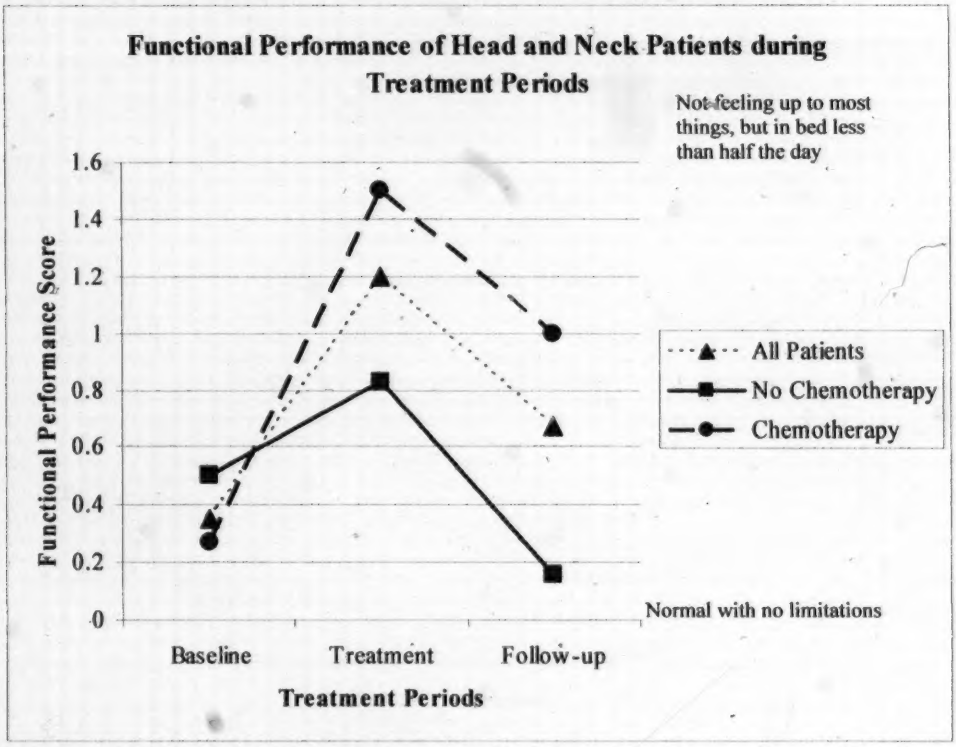

Figure 4.3 Functional performance score patterns of Head and Neck Cancer Patients during treatment periods: No Chemotherapy Group vs Chemotherapy Group. Using repeated measures analysis of variance (ANOVA) that in All patients- from Baseline to Treatment ($p<0.0001$); from Treatment to Follow-up ($p<0.001$). No Chemotherapy Group - from Treatment to Follow-up ($p<0.01$). Chemotherapy Group - from Baseline to Treatment ($p<0.0001$); from Treatment to Follow-up ($p<0.03$); from Baseline to Follow-up ($p<0.0001$).
Independent t-test showed that on average during Treatment and Follow-up, patients in the Chemotherapy Group had poorer functional performance ($1.4\pm0.7, p<0.001$; 0.95 ± 0.57, $p<0.0001$, respectively), than patients in the No Chemotherapy Group (0.84 ± 0.37; 0.16 ± 0.38).

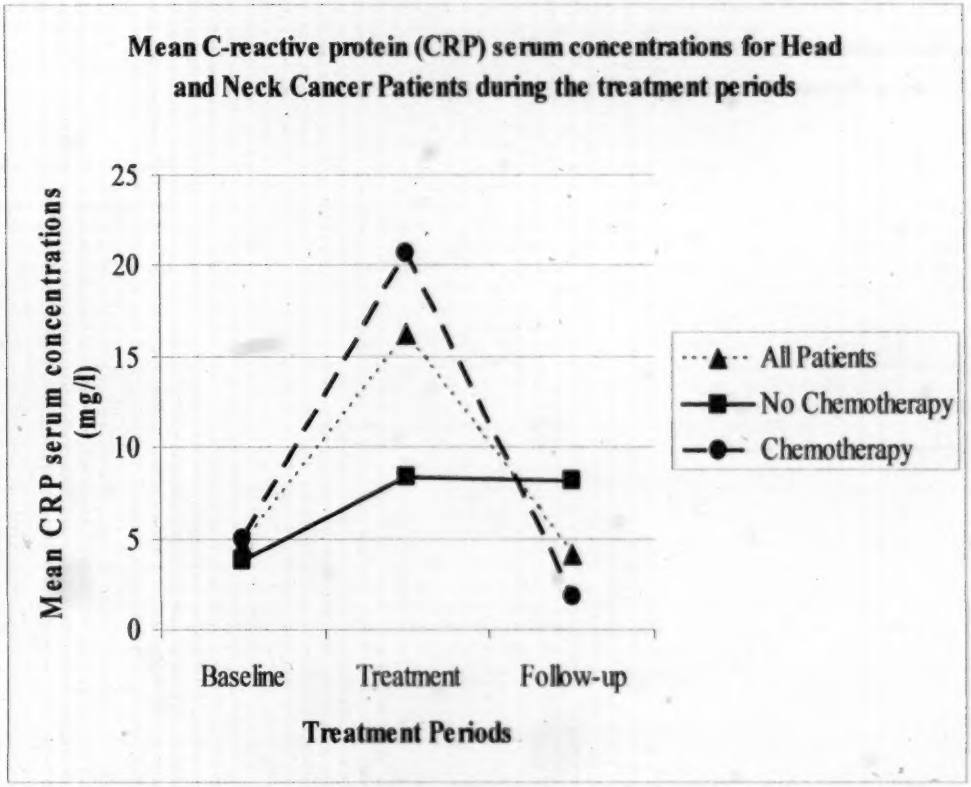

Figure 4.4 Mean C-reactive protein (CRP) serum concentration patterns during treatment periods for Head and Neck Cancer Patients: No Chemotherapy Group vs Chemotherapy Group. Using repeated measures analysis of variance (ANOVA) for All Patients: Baseline to Treatment ($p<0.0001$); Treatment to Follow-up ($p<0.0001$). No Chemotherapy Group: no significant differences between treatment periods. Chemotherapy Group: Baseline to Treatment ($p<0.0001$), Treatment to Follow-up ($p<0.0001$).
Independent t-test showed that on average during Treatment, patients in the Chemotherapy Group had increased CRP concentrations (21.4 ± 23.4mg/l;$p<0.032$), than patients in the No Chemotherapy Group (7.9 ± 13.4mg/l).

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CHAPTER 5

5.1 SUMMARY

In 1859, Florence Nightingale wrote that "every careful observer of the sick will agree with this, that thousands of patients are annually starved in the midst of plenty".[1] Over a century later, involuntary weight loss is still a common occurrence in patients, especially cancer patients and those with HNC, despite numerous opportunities for modern nutritional intervention. Advanced nutritional screening tools, oral enteral nutrition supplements and artificial feeding with gastrostomy tubes are just a few of the modern treatment options unavailable to Miss Nightingale.

In the last decade marked advances in the treatment of HNC have improved tumour control rates and survival. However, while these advances have improved the treatment of the cancer(s), they have also been associated with a higher occurrence of weight loss. In addition to treatment, numerous other factors may contribute to involuntary weight loss in HNC patients. These include symptoms like loss of appetite, dysphagia, alterations in dietary intake, and metabolic changes. Attempts to ameliorate the weight loss with oral enteral nutrition supplements and artificial feeding have had limited success.

Like Miss Nightingales'- "Notes on Nursing", the object of this thesis project was to address clinical problems, in this case, the nutritional status of HNC patients. I accomplished this by evaluating nutritional screening tools; by using the nutritional screening tool deemed most reliable and valid to evaluate the nutrition status of HNC patients prior to treatment; by evaluating the relationship between symptoms and reduced dietary intake, weight loss, and reduced functional capacity; and by

evaluating the relationship between types of treatment and symptoms, systemic inflammation, dietary intake, weight loss, functional performance, and quality of life in HNC patients over time.

This chapter focuses on answering the three important questions arising from this work: who should be responsible for the implementation of nutritional screening?; what are the conditions and criteria for the implementation of artificial feeding?; and which symptoms are correctable or modifiable?

5.2 WHO SHOULD BE RESPONSIBLE FOR THE IMPLEMENTATION OF NUTRITIONAL SCREENING?

The conclusions under this heading are based on the following findings:

- At presentation, over half (55%) of the patients were at nutritional risk (PG-SGA score ≥ 4) and 30% (107/350) were in critical need of nutritional intervention (PG-SGA score ≥ 9). Forty-eight percent of the patients had Grade 1 weight loss at presentation. At treatment the mean percentage weight loss for all patients was -9.4%. Patients' caloric intake declined from baseline energy intakes of 2500 ± 618 kcal to 1550 ± 1009 kcal during treatment. Symptoms with potential to influence nutritional intake were common before, during, and after treatment. These symptoms, affected patients' dietary intake and were associated with weight loss, reduced functional performance and quality of life.

The successful management of involuntary weight loss begins with the systematic identification of nutritional risk, but the implementation of a suitable approach is hindered by several factors. In clinical practice, time and lack of resources often

prevent the completion of a thorough nutrition assessment on each patient by a dietician. Also, the responsibility for the management of involuntary weight loss is often ambiguous, as it is within the domains of medicine, nursing, and dietetics. As with many ambiguously defined domains of practice, many professionals may opt to not complete an assessment, assuming it will be undertaken by a colleague, thus, leaving a "gap in care", and leaving patients at nutritional risk for malnutrition. Therefore, I suggested in paper 1 that because nurses have access to patients on admission to ambulatory clinics at cancer centers, they are in an ideal position to perform routine nutrition screening. Additionally, the responsibility to monitor adequate nutrition is a nursing responsibility, as are nutrition-related patient outcomes such as measurement of height and weight, evaluation of current diet, and assessment of symptoms, general appearance, mental status, and functional ability.

Although the primary purposes of nutritional screening tools is to ensure a standardized approach for referral of patients identified with a nutritional risk to the dietician, nutritional screening tools can also formalize boundaries of responsibilities between the dietician, nurse, and physician, and assist in defining a standardized method of nutritional assessment of patients.[2] Having a standardized method of nutritional assessment is also essential for nutrition-related research. In our institution, the Patient Generated Subjective Global Assessment (PG-SGA) nutrition screening tool not only defines a standardized interventional approach to the nutrition care of patients but it is also used to gather information for a database from which research can be done. The nutrition profile of head and neck cancer patients presented in paper 2 was based on the data collected from the PG-SGA.

Since the scope of responsibility of nurses includes nutritional screening and monitoring the nutrition status of patients, knowledge of nutrition, nutrition screening tools, and nutritional assessments is required. Therefore, substantive nutrition education should be incorporated into the undergraduate and graduate nursing education programs.

5.3 WHAT ARE THE INDICATIONS AND CRITERIA FOR THE IMPLEMENTATION OF ARTIFICIAL FEEDING?

- At presentation, HNC patients are strikingly heterogeneous with respect to weight, body mass index, and weight loss history. Patients receiving adjuvant chemotherapy had cumulative body weight losses upwards of 23% within a 20 week period, whereas patients not receiving chemotherapy had cumulative body weight losses of 13% over that same time period. The cumulative energy deficits of patients not receiving chemotherapy could be in the order of 30,313 kcal in a 20 week period, while patients receiving adjuvant chemotherapy may have had cumulative energy deficits upwards of 122,640 kcal over the same time period. For all patients, the frequency of symptoms nearly quadrupled at T2 (during treatment) compared to that at T1 (baseline). During treatment, ~60% of all patients energy intake was derived from oral nutritional supplements and/or other liquids and mean energy intake was 20.3 ±2.4 kcal/kg/d. During treatment, the functional performance and quality of life significantly declined in patients receiving adjuvant chemotherapy

The indications and criteria for artificial feeding of head and neck cancer patients are plagued by controversy. The principle factors contributing to the controversy stem from the lack of clear evidence that artificial feeding ameliorates weight loss and offers significant benefit to the survival of HNC patients. Another issue is based the concern that artificial feeding may contribute to the loss of swallowing function. Consequently, physicians are reluctant to make the decision to provide artificial feeding or simply (choose to) delay it, leaving many patients with significant energy deficits which are difficult to "make up".

Other endpoints in the decision to provide artificial feeding that warrant consideration include the ability to maintain adequate dietary intake and hydration, risk and consequences of malnutrition, and quality of life. Our results show that patients receiving adjuvant chemotherapy and patients with dysphagia ($\leq$ 10ml/min) were unable to maintain adequate oral intake and as such, were at high risk for malnutrition, and had significantly reduced functional ability and quality of life during treatment. It is well recognized that malnutrition results in the loss of lean tissue mass, the loss of muscle strength, and impaired wound healing (ie, fistula development and increased rejection of skin and bone grafts). Artificial feeding offers the possibility of increasing the patients energy intake, and reducing their risk of malnutrition. The benefits of artificial feeding have been demonstrated in surgical and critical care patients; clinical evidence shows that artificial feeding improved wound healing and resistance to infection, prevented loss of lean tissue, enhanced recovery time, and improved quality of life.[3,4] While we could expect to see similar outcomes in HNC patients, further studies would be required. Future studies evaluating the

efficacy of artificial feeding to improve dietary intake, enhance recovery from treatment, and improve wound healing in head and neck cancer patients would establish whether artificial feeding was of benefit to patients. These studies should include evaluation of the effect of artificial feeding on the maintenance of lean tissue through computerized tomography or dual energy x-ray absorptiometry scanning.

The decision to initiate artificial feeding and the type of oral enteral formula to be delivered is in the hands of the physician and dietician, respectively. However, the care, maintenance, delivery, education, and support of nutritional supplements through the artificial feeding device are the responsibility of the nurse. The goal of the nursing care for the HNC patient with artificial feeding should include promotion of swallowing function to prevent long-term artificial feeding dependence. Therefore, if there is doubt or concern regarding the maintenance of the swallowing function the nurse should make the appropriate referrals to a speech and language pathologist.

5.4 Which symptoms are correctable or modifiable?

- At presentation, 44% of the patients had ≥ 2 symptoms. The most common symptoms were problems swallowing and pain. Loss of appetite, pain, problems swallowing, mucositis, xerostomia, and chemosensory function were exacerbated during treatment. Nearly 50% of all patients still had clinically significant symptoms at follow-up. Many symptoms were significantly associated with energy intake, weight loss, functional performance, and quality of life.

The findings in our studies suggest that certain symptoms contribute to the involuntary weight loss of HNC patients. We also found that the incidence of

symptoms changed over the course of treatment. In order to decrease weight loss, it is important to consider whether these symptoms are modifiable. Pain and mucositis for example, are correctable symptoms. It is possible that with the judicious use of pain-relieving therapies and mucosal protectants that the effects of these symptoms can be relieved or minimized sufficiently to improve dietary intake. On the other hand, chemosensory problems are more difficult to correct and treat. Although suggestions for alterations in food choices and modifications to the diet can be made, in the end it may be up to the patient to discover through trial and error the foods they find appealing.

The optimal management of symptoms is dependent on thorough and frequent evaluations by the nurse. However, the comprehensive evaluation of the numerous symptoms experienced by the HNC patient is time consuming and exhausting for the patient. Additionally, patients may be reluctant to complain about symptoms believing that others are more deserving of the nurses' attention.[5] Therefore, to address the needs of HNC patients, I suggest that a designated specialist with expertise in head and neck cancer be responsible for providing support, coordination and continuity of care throughout the trajectory of treatment. The responsibilities would include patient education, symptoms assessment and management (pre-treatment and bi-weekly treatment and follow-up reviews), evaluation of weight and diet (pre-treatment and bi-weekly treatment and follow-up reviews), co-ordination of information sessions, assessments, and appointments with dietician, speech-language pathologist, dentist (denturist), physiotherapist, and physicians.

Currently, nurses are being placed in the role of HNC clinical nurse specialist to provide support for HNC patients and their family.[6,7] Wiederholt, Connor, Hartig, & Hariri[7] described the position of the head and neck nurse coordinator as case managers, who bridge the gap in care between the patient and the multidisciplinary health care team. As case managers, the nurses are responsible for assessments, symptom management, providing support care including management of dehydration and malnutrition, and education to the head and neck patient and their family. The authors reported that head and neck nurse coordinators have improved the quality of life of head and neck cancer patients by providing them with coordinated and continuous care. Future studies could assess the effectiveness of clinical nurse specialist led care in the management of HNC patients. Future intervention studies are also needed to evaluate clinical guidelines for nursing care of HNC patients.

Head and neck cancer patients experience multiple symptoms due to the location of the tumour and the effects of treatment. Furthermore, our results suggest that symptoms significantly influence dietary intake of HNC patients. Ideally, all symptoms impacting dietary intake throughout the course of treatment should be evaluated. A recent review identified twenty-one symptom assessment instruments that were suitable to evaluate patient symptoms.[8] However, none of symptom assessment instruments evaluated a symptoms' impact on dietary intake. Therefore, to optimize the assessment of symptoms that have an impact dietary intake, the development of an instrument that evaluates numerous symptoms, is easy to use and understand, and is applicable to clinical practice and research would be of value. Future research would be needed to validate this assessment instrument.

Future research studies should also concentrate on symptom management of pain, dysphagia, and loss of appetite, as they would be useful in establishing guidelines for nutritional care of the HNC patient.

At present, involuntary weight loss is a continuing issue in cancer patient, and in HNC patients. The development of clinical strategies for addressing the nutritional issues of involuntary weight loss in head and neck cancer patients include knowing who should conduct and be accountable for nutritional screening and nutrition referrals, knowing who should be targeted for nutritional interventions, and knowing where to focus nutritional interventions. It is my greatest hope that the results of this research project will lead to improvements in these areas, since the aim of nursing is to help patients achieve the best health outcomes possible.

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APPENDIX A

INFORMATION SHEET

An evaluation of food intake and barriers to food intake of head and neck cancer patients before, at the end, and six weeks after radiation therapy or chemotherapy

(Nutritional Status and Barriers to Dietary Intake in Head and Neck Cancer Patients Prior to, on Completion of, and Six Weeks after Oncology Treatment)

CONSENT FORM

This form is part of the process of informed consent. It is designed to explain this research study and what will happen to you if you choose to be in this study.

If you would like to know more about something mentioned in this consent form, or have any questions at anytime regarding this research study, please be sure to ask your doctor or nurse. Read this consent form carefully to make sure you understand all the information it provides. You will get a copy of this consent form to keep. You do not have to take part in this study and your care does not depend on whether or not you take part.

Your doctor has given us permission to ask you to be in this study.

Your participation in this study is entirely voluntary. Please take your time to make your decision. It is recommended that you discuss with your friends and/or family about whether to participate in this study.

"WHY IS THIS STUDY BEING DONE?"

You are being asked to take part in this study because you have head and neck cancer and are undergoing radiation therapy or chemotherapy.

Head and neck cancer patients often have difficulty meeting their nutritional needs while undergoing radiation therapy or chemotherapy. Tumour location and side-effects of radiation therapy or chemotherapy including dry mouth, mouth sores, difficulty chewing and swallowing, changes in taste and smell, and loss of appetite lead to poor food intake and weight loss. Weight loss is associated with treatment delays, hospitalization, and reduced quality of life in patients with head and neck cancer. This study is being done because head and neck cancer patients are often at risk for weight loss during the course of radiation therapy or chemotherapy. Currently, there is no clear understanding of how side effects of cancer treatment affect nutrition status and food intake of patients with head and neck cancer. A number of tests that examine swallowing, dry mouth, mouth sores, and taste and smell function will be used to evaluate their effect on nutrition status and food intake of head and neck cancer patients.

"WHAT DO WE HOPE TO LEARN?"

We hope to learn more about how side-effects of radiation therapy or chemotherapy affect nutrition status and food intake in head and neck cancer patients.

The purpose of this study is to evaluate the nutrition status, food intake, and quality of life of head and neck cancer patients before, at the end, and 6 weeks after treatment. The secondary objectives of the study are to assess the side effects of radiation therapy or chemotherapy and determine if they affect nutrition status, food intake, and quality of life of head and neck cancer patients before, at the end, and 6 weeks after treatment.

"WHAT IS INVOLVED IN THIS STUDY?"

In this study, you will undergo an evaluation of nutrition status, food intake, quality of life, swallowing, dry mouth, mouth sores, and taste and smell function at the Cross Cancer Institute. All of these evaluations are described below.

"HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?"

About 100 people with head and neck cancer having radiation therapy or chemotherapy will take part in this study.

"WHAT WILL MY PARTICIPATION INVOLVE?"

If you take part in this study, you will have the following tests:

Test or Questionnaire	Before Treatment	At the end of Treatment	6 weeks after Treatment
A. Patient Generated-Subjective Global Assessment (PG-SGA)	X	X	X
B. Blood Test	X	X	X
C. 3-day Dietary Record	X	X	X
D. 24-hour urine collection	X	X	X
E. University of Washington Quality of Life Questionnaire- Revised (UWQOL-R)	X	X	X
F. Head and Neck Patient Symptom Checklist	X	X	X
G. Timed Swallowing Test	X	X	X
H. Xerostomia Grading	X	X	X
I. Mucositis Scoring	X	X	X
J. Taste and Smell Survey	X	X	X

A. Patient Generated-Subjective Global Assessment (PG-SGA). The PG-SGA is a screening tool used to assess your nutritional status based on your weight history and activity level. This questionnaire will take about 5 minutes to complete.

B. Blood Tests. For this study you will be required to provide blood samples. The blood tests will be used to assess your nutrition status. The blood samples will be drawn by trained laboratory staff at the Cross Cancer Institute. The blood sample should take about 30 minutes.

C. 3-day Dietary Record. The purpose of the dietary record is to examine what you are eating and drinking. This record will then be used to analyze the quality and quantity of the nutrients in your diet. You will be provided with instructions and material to complete a 3-day dietary record (approximately 30 minutes per day). To complete the dietary record, you will be asked to record everything you eat and drink for a total of 3 days. It is important that you do not alter your diet during this period of time; rather, you should eat as you would normally do if you were not recording your dietary intake. A sample day is provided with the instructions so that you understand the importance of the details required in filling out the record. During the time you are completing the dietary record, the study coordinator will contact you by telephone to ensure that you do not have any further question in completing the record. After you have completed the dietary records you will be asked to return them in person during your scheduled appointment at the Cross Cancer Institute.

D. 24-hour Urine Collection. The purpose of the 24-hour urine collection is to measure the amount of urea excreted by your kidneys as a result of protein metabolism. We will compare the amount of urea excreted by your kidneys to your reported protein intake from the 3-day dietary record. You will be given a special container to collect your urine. You will begin your 24-hour urine collection after the third day of your diet recording period. The first urine you pass on the day you begin urine collection will be flushed down the toilet. Record the time and date this was done on the collection container. The rest of the urine you pass will be collected in the collection container. It is important that you do not touch the urine with toilet paper or a bowel movement, because this results in an unusable sample. Once you have completed the 24 hour urine collection you will be asked to return the container to the laboratory at the Cross Cancer Institute.

E. University of Washington Quality of Life Questionnaire- Revised (UWQOL-R). The purpose of the UWQOL-R is to assess your quality of life. The UWQOL-R asks about your health and quality of life over the last 7 days. This questionnaire takes about 5 minutes to complete.

F. Head and Neck Patient Symptom Checklist. The purpose of the symptom checklist is to assess 17 symptoms that may affect food intake. The Head and

Neck Patient Symptom Checklist asks how often you have experienced each symptom and how much each symptom interferes with your eating. The Head and Neck Patient Symptom Checklist is to be completed in combination with the 3-day dietary record. This questionnaire takes about 5 minutes to complete.

G. Timed Swallowing Test (TST). The purpose of the timed swallowing test is to assess your ability to swallow. The TST involves a questionnaire that asks you to about your swallowing ability and a timed swallowing test. You will first be observed drinking about a teaspoon of water. If you have any problems drinking this amount of water the testing is stopped. If you do not have problems, you will then be observed drinking about 3 fl oz of water over 1 minute. Again, if you have any problems drinking this amount of water the testing is stopped. The questionnaire and testing takes about 15 minutes to complete.

H. Xerostomia Grading. The purpose of the xerostomia (dry mouth) grading is to assess saliva flow. The xerostomia grading involves saliva collection. At least 1 hour before saliva collection, you are asked not to eat, drink, or chew gum. At the time of saliva collection, you will sit in an upright position, with eyes open, swallow, and then after swallowing you will then bend your head forward and allow saliva to collect in your mouth for 5 minutes. Saliva is collected with a tool that resembles an eye dropper. The testing takes about 10 minutes to complete.

I. Mucositis Scoring. The purpose of the mucositis (mouth sores) scoring is to assess the colour of your mouth tissue, for mouth bleeding, and for the presence of mouth sores. For the mucositis assessment you will be asked to sit in an upright position, and then asked to open your mouth so that the inside of your mouth can be assessed. The assessment takes about 5 minutes.

J. Taste and Smell Survey. The Taste and Smell Survey asks you about your senses of taste and smell. The survey will take about 10 minutes to complete.

"HOW LONG WILL I BE INVOLVED IN THE STUDY?"

You may be in this study for 14 weeks, which includes the testing before your cancer treatment, as well as the 2 testing periods at the end, and 6 weeks after your cancer treatment. Each testing period will take about 1.5 hours. The testing will be done at the Cross Cancer Institute during your scheduled appointment visits.

"WHAT ARE THE SIDE EFFECTS?"

You may feel some discomfort from the needle when the blood is drawn. There is also a small risk of fainting, swelling, bruising, bleeding or (rarely) local infections at the site of the needle puncture.

"WHAT ARE MY ALTERNATIVES?"

You may choose not to participate in this study.

"ARE THERE ANY BENEFITS TO PARTICIPATING IN THIS STUDY?"

Participation in this study may or may not be of personal benefit to you. However, based on the results of this study, it is hoped that, in the long-term, patient care can be improved.

"CAN I WITHDRAW FROM THIS STUDY?"

Taking part in this study is voluntary; you may withdraw from the study at any time if you wish to do so.

"ARE THERE COSTS TO ME FOR TAKING PART IN THIS STUDY?"

You will not have to pay for the testing you receive in this study. Your scheduled appointment at the Cross Cancer Institute will take longer than if you were not part of this study. There may be additional costs for taking part in this study, such as parking and transportation, which you will have to pay.

"WHAT ARE MY RIGHTS AS A PARTICIPANT?"

It is important to note that nothing said in this consent form alters your legal rights to recover damages. However, if you suffer an injury or become ill as a result of participating in this research, you retain all your legal rights to pursue other possible avenues of compensation (e.g. legal action).

"WILL MY PERSONAL INFORMATION BE KEPT CONFIDENTIAL?"

Identifiable health information will be collected during this study. This information may be used by the researchers who are carrying out this study, and may be disclosed to others as described below. Any research proposal to use information that identifies you for a purpose other than this study must be approved in advance by the ACB Research Ethics Board.

Direct access to your identifiable health information collected for this study will be restricted to the researchers who are directly involved in this study except in the following circumstances:

Your identifiable health information may need to be inspected or copied from time to time for quality assurance (to make sure the information being used in the study is accurate) and for data analysis (to do statistical analysis that will not identify you). The following organizations may do this inspection:

- Alberta Cancer Board Research Ethics Board, the institutional review board at this centre

Any disclosure of your identifiable health information will be in accordance with the Alberta Health Information Act. As well, any person from the organizations looking at your records on-site at the Cross Cancer Institute will follow the relevant Alberta Cancer Board policies and procedures that control these actions. Any disclosure of your identifiable health information to another individual or organization not listed here will need the approval of the Alberta Cancer Board Research Ethics Board.

Your identifiable health information collected as part of this study is **medical information taken at the Cross Cancer Institute which includes your age, gender, height, weight, other medical conditions, previous surgery, previous radiation therapy, type of cancer, tumour site, tumour stage, treatment method, dosage of radiation, area of radiation exposure, type of radiation therapy, type of chemotherapy, and medications that you are taking** will be kept confidential in a secure Alberta Cancer Board facility.

The researchers who are directly involved in your study may share information about you with other researchers, but you will not be identified in that shared information except by a number. The key that indicates what number you have been assigned will be kept secure by the researchers directly involved with your study and will not be released.

Although absolute confidentiality can never be guaranteed, the Alberta Cancer Board will make every effort to keep your identifiable health information confidential, and to follow the ethical and legal rules about collecting, using and disclosing this information in accordance with the Alberta Health Information Act and other regulatory requirements.

"WHO DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?"

For information about your disease and/or research related injury/illness, you may contact the Principal Investigator Vickie Baracos, 432-8232, or page her through the Cross Cancer Institute Switchboard at (780) 432-8771 to answer any questions you have about this study.

If you feel, at any time, that you have not been informed to your satisfaction about the risks, benefits, or alternatives of this study, or that you have been encouraged to continue in this study after you wanted to withdraw, you can call the Patient Representative at (780) 432-8585.

UNDERSTANDING OF PARTICIPANTS

I can refuse to take part or withdraw from this study at any time without jeopardizing my health care. If I continue to take part in the study, I will be kept informed of any important new developments and information learned after the time I gave my original consent.

I also give consent for the Principal Investigator and the Alberta Cancer Board (the Custodian) to disclose identifiable health information, as per the Alberta Health Information Act, to the organizations mentioned on the previous page.

I have read and understood all of the information in this consent form. I have asked questions, and received answers concerning areas I did not understand. I have had the opportunity to take this consent form home for review and discussion. My consent has not been forced or influenced in any way. I consent to participate in this research study. Upon signing this form I will receive a signed copy of the consent.

APPENDIX B

PATIENT-GENERATED SUBJECTIVE GLOBAL ASSESSMENT TOOL

1. Weight
In summary of my current and recent weight:

My current weight is about _____ lbs (kg)

I am about _____ ft (cm)

One month ago I weighed about _____ lbs (kg)

Six months ago I weighed about _____ lbs (kg)

During the past two weeks my weight has:

☐ decreased ☐ not changed ☐ increased

2. Food Intake: As compared to my normal intake, I would rate my food intake during the past month as:

☐ unchanged
☐ more than usual
☐ less than usual

I am now taking:

☐ *normal food* but less than normal amount
☐ little solid food
☐ only liquids
☐ only nutritional supplements
☐ very little of anything
☐ only tube feedings or only nutrition by vein

3. Symptoms: I have had the following problems that have kept me from eating enough during the past two weeks (check all that apply):

☐ no problems eating
☐ no appetite, just did not feel like eating
☐ nausea
☐ constipation
☐ mouth sores
☐ things taste funny or have no taste
☐ problems swallowing
☐ pain; where?_____
☐ vomiting
☐ diarrhea
☐ dry mouth
☐ smells bother me
☐ feel full quickly
☐ Other **_____

** Examples: depression, dental problems, money

4. Activities and Function: Over the past month, I would generally rate my activity as:

☐ normal with no limitations

☐ not my normal self, but able to be up and about with fairly normal activities

☐ not feeling up to most things, but in bed or chair less than half the day

☐ able to do little activity and spend most of the day in bed or chair

☐ pretty much bedridden, rarely out of bed

APPENDIX C

THREE DAY DIET RECORD

THREE-DAY DIETARY INTAKE RECORD

Record Dates: Day 1_____ Day 2_____ Day 3 _____

INSTRUCTIONS FOR RECORDING DAILY FOOD INTAKE

The purpose of this study is to discover everything you eat and drink during a three-day period. It is important to record ALL foods and beverages – whether it is a full course meal at home or a quick can of pop at school. Before you start recording your intake, please read the following instructions and the Sample Day.

The Three-Day Dietary Intake Record has a separate section for every day (see Day 1, Day 2, Day 3 on top each page). Each day is broken up into 6 eating times:

1. Morning meal 2. Midmorning snack 3. Afternoon snack
5. Evening meal 4. Midday meal 6. Evening snack

It is a good idea to carry your Dietary Intake Record book with you and record your entries as soon after eating as possible. Foods and beverages consumed away from home – at school, at the mall, at a restaurant- are just as important as those eaten at home. Please include the following information on your food record:

1. **FOOD AND BEVERAGE ITEMS** Column: Enter all foods and beverages consumed at the meal or snack time. Please record the specific type of food (for example: *WHOLE WHEAT* bread, *FROSTED FLAKES* cereal). In the same column, record all toppings or items added at the time of eating (for example: sugar, syrup, jam, butter, mayonnaise, gravy, milk, salt, etc.). For combination foods, please include detailed information on each item. For example: If you had a tuna sandwich, you would list the following foods and include detailed information for each of them: white bread, mayonnaise, celery, solid white tuna, salt.
2. **DESCRIPTION OF ITEM** Column: For every food or beverage item listed, include the following (if applicable):
   - **Brand**: *MIRACLE WHIP* mayonnaise, *PIZZA HUT DEEP DISH* pizza, *OREO* cookie
   - **Type of flavour**: *BLUEBERRY* muffins, *STRAWBERRY* yogurt
   - **Method of cooking**: *FRIED, BAKED, BBQ'D, HOMEMADE*
   - **All other relevant information included on food label:** *LOW FAT* ranch salad dressing, *28% M.F. (MILK FAT)* cheddar cheese, *LEAN* Ground Beef
3. **UNIT OF MEASURE** Column: For every item consumed, enter the unit of measure you are using for this item. For example: enter the word "cup", "grams", "piece", "ounce", "number", "teaspoon", or "tablespoon". Enter a unit of measure not only for the menu item, but for toppings or items added as well. Each entry must have its own unit of measure. Use measuring cups and spoons whenever possible.
4. **NUMBER OF UNITS** Column: In this area, record the number of units consumed. Include the amount of the food or beverage item and the amount of any topping or items added.

Fill in the two blanks on the bottom of each record. Indicate the time of your meal or snack and where it was eaten (for example: at home, at a restaurant, in class). If you did not eat a meal or snack, please place a check mark (✓) in the space provided on the bottom of the page, so that we do not think you forgot to record it.

Daily check: in the evening, after you have recorded everything for the day, go back over your entries to make sure you have included as much detail as possible for each item. Also check to ensure the blanks are completed on the bottom of the page.

All foods and beverages you consume every day are important and your Dietary Intake Record should be as accurate as possible. It should also reflect the way you usually eat. Please do not change your normal eating habits for the 3 days you are recording your food intake. Your honesty is crucial to the success of this research study.

Thank you for your participation and cooperation in helping with this study. Please look closely at the Sample Day before beginning your Dietary Intake Record. **If you have any questions about filling out your Three-Day Dietary Intake Record, please phone: _____**

Sample Day

FOOD AND BEVERAGE ITEMS	DESCRIPTION OF ITEM	UNIT OF MEASURE	NO. OF UNITS
Enter all foods and beverages consumed. For combination foods, please include detailed information on each item.	Include a detailed description of each food and drink item consumed including: - Brand name - Flavour - Method of cooking - All other relevant information on food/drink label	Enter unit of measure: for example: cup, grams, ounce, piece, teaspoon, tablespoon	Enter number of units
Spaghetti with tomato/meat sauce:			
Pasta	Spaghetti, cooked	Cup	2
Tomato sauce	Hunt's canned sauce, roasted garlic flavour	Cup	1
Meat balls	Made with extra lean ground beef	Number (1 oz/ball)	5
Parmesan cheese, grated	Kraft, 30% Milk Fat (M.F.)	Tablespoon	1
Garlic Bread:			
Italian Bread	Toasted	Piece (large slice)	3
Garlic Butter		Teaspoon	3
Caesar salad:			
Lettuce	Romaine	Cup	1
Croutons	Safeway brand, garlic flavor	Tablespoon	2
Bacon bits	Simulated flavour, No Name Brand	Tablespoon	2
Caesar salad dressing	Kraft, Fat free	Tablespoon	2
Milk	1%	Cup	1
Tiramisu	Sarah Lee	Slice	1
Coffee	Black	Cup	1

Fill in blanks: Time of meal/snack: 6:00 pm **Location meal/snack was consumed:** at home

Please CHECK (✓) if you did not eat or drink at this meal or snack time:_____

APPENDIX D

REVISED UNIVERSITY OF WASHINGTON QUALITY OF LIFE QUESTIONNAIRE

This questionnaire asks about your health and quality of life over the past seven days.
Please answer all the questions by checking one box for each question.

1. **Pain.** (check one box)
☐ I have no pain
☐ There is mild pain not needing medication.
☐ I have moderate pain-requires regular medication (codeine or nonnarcotic)
☐ I have severe pain controlled only by narcotics.
☐ I have severe pain, not controlled by medication.

2. **Appearance.** (check one box)
☐ There is no change in my appearance.
☐ The change in my appearance is minor.
☐ My appearance bothers me but I remain active.
☐ I feel significantly disfigured and limit my activities due to my appearance.
☐ I cannot be with people due to my appearance.

3. **Activity.** (check one box)
☐ I am as active as I have ever been.
☐ There are times when I can't keep up my old pace, but not often.
☐ I am often tired and have slowed down my activities although I still get out.
☐ I don't go out because I don't have the strength.
☐ I am usually in bed or chair and don't leave home.

4. **Recreation.** (check one box)
☐ There are no limitations to recreation at home or away from home.
☐ There are a few things I can't do but still get out and enjoy life.
☐ There are many times when I wish I could get out more, but I'm not up to it.
☐ There are severe limitations to what I can do. I stay at home and watch TV.
☐ I can't do anything enjoyable.

5. **Swallowing.** (check one box)
☐ I can swallow as well as ever.
☐ I cannot swallow certain solid foods.
☐ I can only swallow liquid food.
☐ I cannot swallow because it "goes down the wrong way" and chokes me.

6. **Chewing.** (check one box)
☐ I can chew as well as ever.
☐ I can eat soft solids but cannot chew some foods.
☐ I cannot even chew soft foods.

7. **Speech.** (check one box)
☐ My speech is the same as always.
☐ I have difficulty saying some words but I can be understood over the phone.
☐ Only my family and friends can understand me.
☐ I cannot be understood.

8. **Shoulder.** (check one box)
☐ I have no problem with my shoulder.
☐ My shoulder is stiff but it has not affected my activity or strength.
☐ Pain or weakness in my shoulder has caused me to change my work.
☐ I cannot work due to problems with my shoulder.

9. **Taste.** (check one box)
☐ I can taste food normally.
☐ I can taste most food normally.
☐ I can taste some foods.
☐ I cannot taste any foods.

10. **Saliva.** (check one box)
☐ My saliva is of normal consistency.
☐ I have less saliva than normal, but it is enough.
☐ I have too little saliva.
☐ I have no saliva.

Which issues have been the most important to you during the past 7 days?

Check up to 3 boxes.

☐ Pain
☐ Appearance
☐ Activity
☐ Recreation
☐ Swallowing
☐ Chewing
☐ Speech
☐ Shoulder
☐ Taste
☐ Saliva

General Questions

Compared to the month before you developed cancer, how would you rate your health related quality of life? (check one box)

☐ Much better
☐ Somewhat better
☐ About the same
☐ Somewhat worse
☐ Much worse

In general, would you say your **health related quality of life** during the past 7 days has been:

☐ Outstanding
☐ Very good
☐ Good
☐ Fair
☐ Poor
☐ Very poor

Overall quality of life includes not only physical and mental health, but also many other factors, such as family, friends, spirituality, or personal leisure activities that are important to your enjoyment of life. Considering everything in your life that contributes to your personal well-being rate your **overall quality of life** during the past 7 days. (check one box)

☐ Outstanding
☐ Very good
☐ Good
☐ Fair
☐ Poor
☐ Very poor

Total Score____

APPENDIX E

HEAD AND NECK SYMPTOM CHECKLIST

Head & Neck Patient Symptom Checklist

Instructions: Below is a list of 17 symptoms. Please circle the number that best describes how often you experienced the symptom **during the past 3 days,** and if it interferred with your eating.

During the past 3 days:	How often did you have this symptom?					Has this symptom interferred with eating?				
Symptom	Not at all	A little bit	Some what	Quite a bit	A lot	Not at all	A little bit	Some what	Quite a bit	A lot
Pain	1	2	3	4	5	1	2	3	4	5
Anxious	1	2	3	4	5	1	2	3	4	5
Dry mouth	1	2	3	4	5	1	2	3	4	5
Loss of appetite	1	2	3	4	5	1	2	3	4	5
Constipation	1	2	3	4	5	1	2	3	4	5
Feeling full	1	2	3	4	5	1	2	3	4	5
Depressed	1	2	3	4	5	1	2	3	4	5
Thick saliva	1	2	3	4	5	1	2	3	4	5
Diarrhea	1	2	3	4	5	1	2	3	4	5
Sore mouth	1	2	3	4	5	1	2	3	4	5
Lack of energy	1	2	3	4	5	1	2	3	4	5
Nausea	1	2	3	4	5	1	2	3	4	5
Difficulty chewing	1	2	3	4	5	1	2	3	4	5
Smells bother me	1	2	3	4	5	1	2	3	4	5
Vomiting	1	2	3	4	5	1	2	3	4	5
Difficulty swallowing	1	2	3	4	5	1	2	3	4	5
Taste changes	1	2	3	4	5	1	2	3	4	5
Other: Specify	1	2	3	4	5	1	2	3	4	5

APPENDIX F

TIMED SWALLOWING TEST

Patient is asked the following questions

At this present time:

1.Do you have a problem with your swallowing? Yes No

2. Do you have difficulty keeping food or drink in your mouth? Yes No

3. Do you have difficulty using your tongue to move food around in your mouth? Yes No

4. Do you have episodes of coughing when eating or drinking? Yes No

5. Does food or drink 'go down the wrong way' (ie) into your breathing tubes? Yes No

6. Are you aware of having to be careful when eating or drinking in case things 'go down the wrong way' into your breathing tubes? Yes No

7. Does food ever get stuck in your throat? Yes No

8. Do liquids come back through your nose when you swallow them? Yes No

9. Do you have any other major medical problems? Yes No

10. a. Do you wear dentures? Yes No

b. If so are they top, bottom, or both? Top Bottom Both

c. Do they fit well? Yes No

11. Do you take any of the following medicine every day?

Antidepressants _____

Minor tranquilizers _____

Major tranquilizers _____

Other drugs_____

Swallowing Procedure

Water Test 1 **5-10 ml water** Patient choking **STOP TEST!**

Water Test 2 **90 ml water** **1 minute**

Amount of residual water _____

Number of Swallows _____ **TIME**_____

APPENDIX G

XEROSTOMIA GRADING

Grading	1	2	3
Subjective; Functional difficulties	No disability	Dryness requiring additional fluids for swallowing	Dryness causing dietary alterations, interference with sleep, speaking, or other activities
Objective; Saliva Flow	Flow > 0.2 ml/min	Flow 0.1-0.2 ml/min	Flow <0.1 ml/min

Saliva Flow _____ml/min

Total Score ____

APPENDIX H

REVISED WESTERN CONSORTIUM FOR CANCER NURSING RESEARCH STOMATITIS STAGING SYSTEM (WCCNR-SSS)

SCORE	LESIONS	COLOUR	BLEEDING
0	None	Pink>50%	None
1	1-4	Slightly red>50%	
2	>4	Moderately red>50%	With eating or mouth care
3	Coalescing lesions on 50% or more of the mouth surface	Very red>50%	Spontaneous-fresh bleeding apparent or dried blood on pillow

Total Score____

APPENDIX I

SELF-PERCEIVED TASTE AND SMELL DYSFUNCTION QUESTIONNAIRE

The purpose of this survey is to assess how cancer affects the senses of taste and smell.

Please answer the following questions as best you can.

Since your diagnosis (T1) or Since you began your treatment of radiation therapy or radiation and chemotherapy (T2) or Since you completed your treatment of radiation therapy or radiation and chemotherapy (T3)

1. Have you noticed any changes in your sense of taste? Yes No

If yes, please describe: _____

_____

2. Have you noticed any changes in your sense of smell? Yes No

If yes, please describe: _____

_____

3. Have you ever noticed that a food tastes different than it used to? Yes No

If yes, please describe: _____

_____

4. Have you ever noticed that a food smells different than it used to? Yes No

If yes, please describe: _____

_____

5. I have a persistent bad taste in my mouth (please (√) the **BEST** answer)

NEVER	RARELY	SOMETIMES	OFTEN	ALWAYS

6. The persistent taste is (please (√) **ALL** that apply)

SALTY	SWEET (LIKE SUGAR)	SOUR (LIKE LEMON)	BITTER (LIKE COFFEE)	OTHER

other (specify) _____

7. Do specific drugs interfere with your sense of taste? Yes No

If yes, which ones? _____

_____

8. Do some drugs taste worse than others? Yes No

If yes, which ones? _____

_____

9. Do specific drugs interfere with your sense of smell? Yes No

If yes, which ones? _____

_____

10. Do some drugs smell worse than others? Yes No

If yes, which ones? _____

_____

11. Comparing my sense of taste now, to the way it was before your diagnosis:

(please (√) in the box that BEST describes your sense of taste):

	STRONGER	AS STRONG	WEAKER	I CANNOT TASTE AT ALL
Salt				
Sweet (ie) sugar				
Sour (ie) lemon				
Bitter (ie) black coffee				

12. Comparing my sense of smell now to the way it was before your diagnosis, odors are

1) stronger

2) as strong

3) weaker

4) I cannot smell at all

13. I would rate my abnormal sense of taste as: (please (√) the BEST answer)

INSIGNIFICANT	MILD	MODERATE	SEVERE	INCAPACITATING

14. How has your abnormal sense of taste affected your quality of life?

15. I would rate my abnormal sense of smell as: (please (√) the BEST answer)

INSIGNIFICANT	MILD	MODERATE	SEVERE	INCAPACITATING

16. How has your abnormal sense of smell affected your quality of life?